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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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SURGERY

VOL. 37 JUNE, 1955 NO. 6

Original Communications

THE PHLEBOGRAPHIC PATHOLOGY OF THE POSTPHLEBITIC LIMB

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VENOUS disease of the lower leg is one of the most widespread and, often, poorly treated diseases today. The basic concepts of therapy of deep vein involvement have not changed in essence since Linton[1] introduced and popularized the "flap operation" in 1938. The understanding of deep vein disease has changed little since the description of deep vein varicosis by Verneuil[2] in 1855.

A phlebographic technique that will give an accurate appraisal of the deep vein pathology was presented by Felder[3] in 1950, and recently improved.[4-8] The use of "isoflow" phlebography[7, 8] allows the investigation of the pathologic anatomy of the postphlebitic syndrome in a large number of cases with ease.

METHOD OF STUDY

In this study, eighty-three phlebographic studies were made in patients with postphlebitic limbs. All cases were subjected to a period of intensive conservative therapy in an attempt to heal any open stasis ulcers prior to the phlebographic study. Those postphlebitic limbs which failed to respond to the conservative regimen were subjected to phlebography. A small number of patients were hospital bed patients at the time of the study, but over 90 per cent of the group were ambulatory.

INTERPRETATION

The films were interpreted using the criteria of Sgalitzer[9] and that further outlined by Felder.[6] Our criteria for valvular incompetency are as follows:

1. Exceptional dilatation of the vein.

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2. One or more incompetent valves in the same area with dilatation of the vein below the valve.
3. Tortuosity.
4. Pooling of contrast medium in dilated deep vein varices.
5. An extensive irregular lumen without visible valve structure.

The finding of one incompetent valve is not considered adequate evidence to label a vein incompetent; however, finding the entire picture described previously does allow one to come to this conclusion.

RESULTS

Table I gives the percentage of visualization of the deep veins of the limbs studied, and the percentage in the group that showed pathology. In this analysis there are a few instances in which a vein was not visualized and thus the status of these remains unknown.

TABLE I. AN ANALYSIS OF THE PHLEBOGRAPHIC FINDINGS FROM 83 STUDIES OF POSTPHLEBITIC LIMBS*

VEIN	PERCENTAGE VISUALIZED		VEIN	PERCENTAGE VISUALIZED	
Femoral		85	Posterior tibial		90
Normal	52.5		Normal	75.0	
Bifid	6.0		Incompetent	15.0	
Incompetent	7.0				
Venous by-pass	18.0		Peroneal		92
Thrombosis	1.5		Normal	77.0	
			Incompetent	15.0	
Deep femoral		54			
Normal	44.0		Sural		84
By-pass	10.0		Normal	54.0	
			Incompetent	30.0	
Long saphenous		65			
Normal	2.0		Short saphenous		23
Incompetent	63.0		Normal	3.5	
			Incompetent	19.5	
Thigh communicators		25			
Normal	5.0		Leg communicators		
Incompetent	20.0		Lateral		92
			Normal	15.0	
Popliteal		92	Incompetent	77.0	
Normal	32.0				
Bifid	52.0		Medial		89
Incompetent	8.0		Normal	8.0	
			Incompetent	81.0	
Anterior tibial		84			
Normal	81.0		Posterior		81
Incompetent	3.0		Normal	9.0	
			Incompetent	72.0	

*All figures represent percentages visualized of the total series.

Femoral Vein.—The femoral vein was visualized in 85 per cent of the series. It was thought to be abnormal in 26.5 per cent. A bifid femoral vein was found in 6 per cent. These were all thought to be physiologically normal. Duplication, such as this, was described by Braune[10] in 1889 from anatomic dissections. An incompetent femoral vein was found in 7 per cent of our studies. A femoral thrombosis was found in one patient, or 1.5 per cent of the series.

"Venous by-passes" were noted in 18 per cent. We have observed two types of by-pass (Fig. 1). One is the large collateral, either of a duplicated

parallel vein or veins running in juxtaposition to the primary channel with many short intercommunications. These we have chosen to call minor by-passes. The second type, or major by-pass, is the large collateral, in another plane, with few or no connections with the primary channel other than its origin and termination. The deep femoral vein is often incorporated in this type of system as brought out by Edwards and Robuck.[12]

Deep Femoral Vein.—The profunda femoris was visualized in 54 per cent of the series; it was incorporated in a venous by-pass in 10 per cent.

Long Saphenous Vein.—The long saphenous vein was visualized in 65 per cent of the cases in spite of attempts to prevent filling of this system. The vein was incompetent in 63 per cent and normal in 2 per cent.

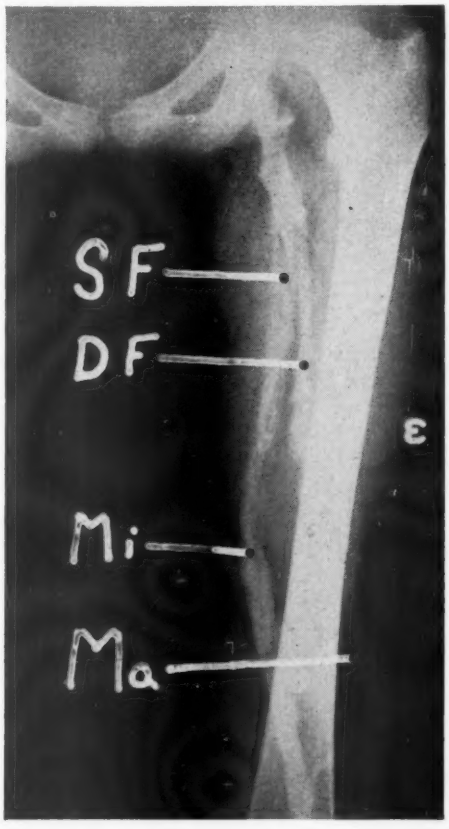

Fig. 1.—Major and minor by-passes of the thigh. *SF,* Superficial femoral vein with *Mi,* minor by-passes. *DF,* Deep femoral veins incorporated in a *Ma,* major by-pass.

Communicating Veins of the Thigh.—Communicating veins of the thigh were noted in 25 per cent of the cases, being normal in 5 per cent and incompetent in 20 per cent. This compares well to the studies of Linton,[1] who found such communicating veins to be present in 25 to 30 per cent of his anatomic studies. These veins were almost always in the medial lower third of the thigh.

Popliteal Veins.—The popliteal vein was visualized in 92 per cent of the series; this vein was incompetent in 8 per cent. There was evidence of a bifid

popliteal vein in 52 per cent. This approximates the data of Williams,[11] who found a bifid or duplicate popliteal vein in 66 per cent of his anatomic dissections. The bifid popliteal vein is felt to be a physiologically normal vein, but is of importance if the popliteal vein is to be ligated, as has been a recent vogue (Fig. 3). In a review by one of us (T. O. M.)* of 60 cases of popliteal vein ligation between 1945 and 1952, no instance of a bifid popliteal vein was mentioned in the operative report, and thus, a bifid popliteal channel must have been missed in many of these cases.

Fig. 2.—Incompetent anterior tibial veins (*AT*). *C*, Communicating veins.

Anterior Tibial Veins.—The anterior tibial veins were visualized in 84 per cent of our series, and were incompetent in 3 per cent (Fig. 2).

*Unpublished data.

Posterior Tibial and Peroneal Veins.—The posterior tibial vein was visualized in 90 per cent of the series. Seventy-five per cent were normal and 15 per cent were incompetent. The peroneal veins were visualized in 95 per cent; 15 per cent were incompetent (Fig. 4).

Sural Veins.—The sural veins were visualized in 84 per cent of the series, of which 30 per cent were incompetent. These veins were often very large and of a "pantaloon" configuration which allowed considerable pooling of the contrast medium (Fig. 5).

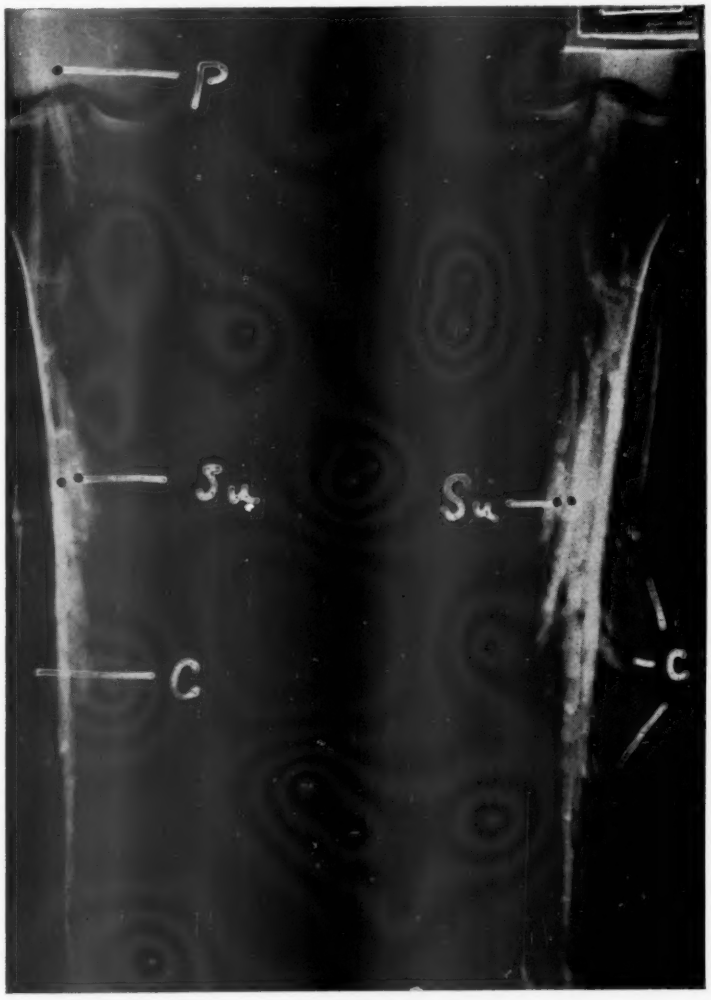

Fig. 3.—Popliteal veins (*P*) with four channels crossing the joint space. *Su*, Sural veins; *C*, communicating veins.

Short Saphenous Vein.—The short saphenous vein was visualized in only 23 per cent of the series, which, as in the case of the long saphenous vein, is a characteristic of this technique. This vein was incompetent in 19.5 per cent of the cases.

Communicating Veins.—The communicating veins of the leg presented the highest degree of incompetency. These veins were divided into lateral, medial, and posterior groups (Figs. 2-5). The lateral group were visualized in 92 per cent of the series. These were normal in 15 per cent and incompetent in 77 per cent. The medial group were visualized in 89 per cent of the series, of which 81 per cent were incompetent. The posterior group were visualized in 81 per cent of the series, being incompetent in 72 per cent.

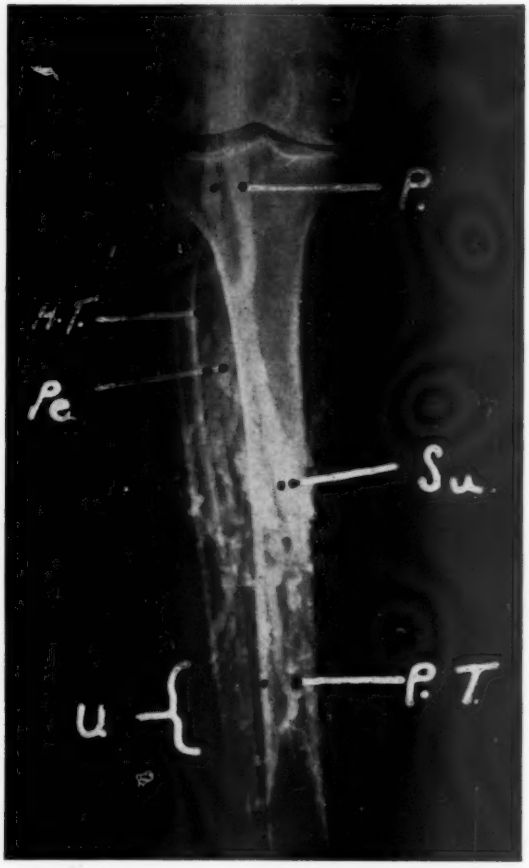

Fig. 4.—Popliteal vein (*P*), anterior tibial veins (*AT*), peroneal veins (*Pe*), ulcer site (*U*), posterior tibial veins (*PT*), sural veins (*Su*).

DISCUSSION

The incidence of venous incompetency seems to be related to the status of supportive structures around the vein. The anterior tibial veins lie in a tight compartment surrounded by bone and fascia. Furthermore, this compartment contains a strong and very active muscle group. This should allow excellent surrounding support to this venous system, and may account for the low incidence of incompetency here (3 per cent). The posterior tibial and peroneal veins lie between the deep muscles of the calf and the interosseous fascia. The degree of support here is not as good as that in the anterior tibial system. The incidence of incompetency increases to 15 per cent. The sural

veins arise in the calf muscles, and, after coursing through these muscles, emerge to join the peroneal, posterior tibial, or popliteal veins. The muscle tone of the posterior calf muscles is often diminished in the older patients, and especially so in the group of patients with postphlebitic limbs. The incidence of incompetency in this area is 30 per cent. The communicating veins of the

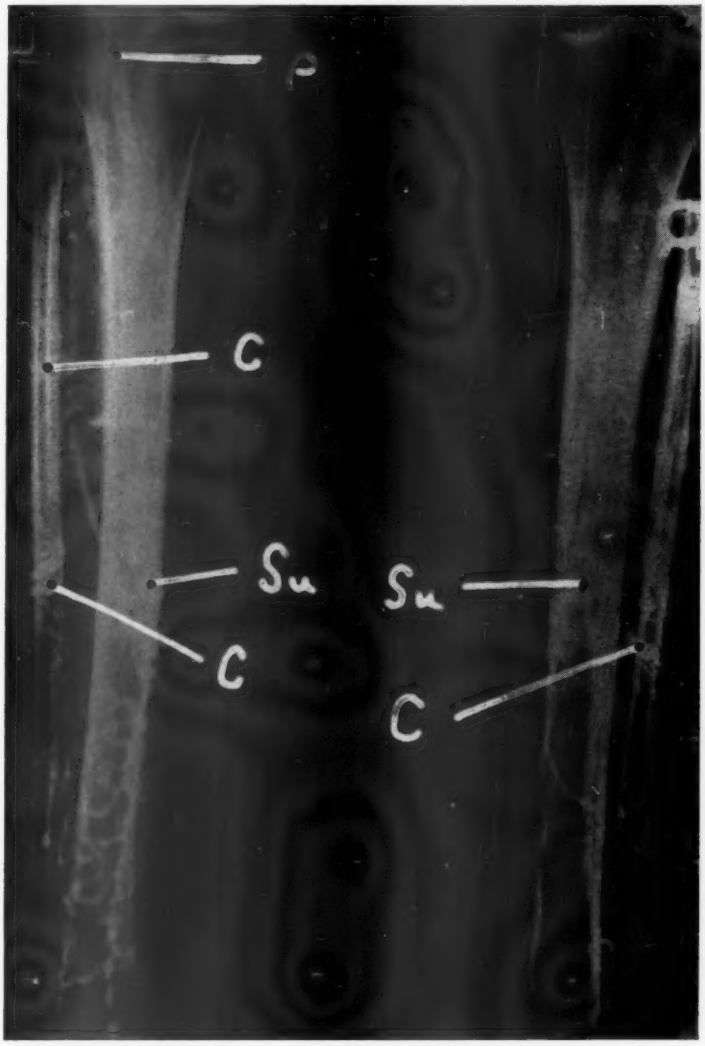

Fig. 5.—Popliteal veins (*P*), communicating veins (*C*), sural veins (*Su*) of a "pantaloon" configuration.

lower leg course through fat and connective tissue to merge with the superficial venous system. These veins have a minimum of support from the surrounding tissue and, as may be expected, have a high degree of incompetency. The high degree of incompetency of these veins further confirms the opinion of Linton[1] as to their importance and the justification for their ligation. It is noted that a high percentage of these medial and posterior communicating

veins take origin from a large incompetent sural system. Many of these veins course for some distance just under the fascia of the posterior calf prior to perforating it to join the superficial system. This indicates that a simple ligation of such a vessel at the point of its fascial perforation still leaves a long, dilated segment of vein open.

It is not our contention that the lack of supporting tone is responsible for the production of an incompetent vein. However, we do feel that failure of muscular support is of importance in the progression of the disease.

The venous by-pass as parallel collateral channels in the thigh, described by Edwards and Robuck,[12] may enlarge as a result of an obstruction of a central channel. We have often found the valves in these by-passes to be incompetent or completely absent. This situation probably exists in many more individuals than we have heretofore realized. If such collaterals disturb the venous hemodynamics by circumvention of vein segments with normal valves, then one may postulate that some clinical disability may arise. These anatomic variations may be responsible for such complaints as those noted in patients with more obvious venous disease. Since this condition involves the large deep veins of the thigh, it is possible that some instances of unexplained, unilateral ankle edema may be due to it.

It has been noted that occlusions in the deep veins of the lower leg are associated with large, incompetent, communicating veins acting as collaterals either temporarily or permanently. It has been common practice to ligate these communicating veins, and also associated superficial veins, at the site of fascial perforation. The long and short saphenous veins may also be a part of this type of involvement. If the ligation of these superficial by-passes is of salutory nature, then, perhaps, ligation of the deep by-passes may be feasible. We have explored and ligated several deep vein by-passes in the leg and thigh.

SUMMARY AND CONCLUSION

An analysis of the pathologic phlebographic anatomy has been presented from eighty-three studies of postphlebitic limbs. The findings have been discussed with an aim toward a better understanding of the disease process and a more rational approach to surgical therapy. It is felt that a more effective treatment of the postphlebitic limb may be devised from such studies as these. The importance of the communicating veins, the sural veins, and the possible importance of venous by-passes in the thigh have been stressed. The degree of incompetency seems to be related to the muscular and fascial support given to the veins.

REFERENCES

1. Linton, R. R.: The Communicating Veins of the Lower Extremity and the Operative Technique for Their Ligation, Ann. Surg. **107:** 582-593, 1938.
2. Verneuil, A.: Du siége réel et primitif des varices du membre inférieur, Gaz. hebd. méd. **2:** 811-815, 1955.
3. Felder, D. A.: A Method of Venography, Radiology **54:** 516-520, 1950.

4. Felder, D. A.: Anatomical-Spatial Relationships of the Deep Veins of the Lower Extremity as a Basis for Venographic Interpretation, Radiology **54**: 521-526, 1950.
5. Felder, D. A.: Anatomical and Clinical Correlations of Phlebography of the Lower Extremities, Thesis, University of Minnesota, Minneapolis, Minnesota, 1952.
6. Felder, D. A.: The Phlebographic Diagnosis and Treatment of the Postphlebitic Syndrome, Radiology **61**: 208-214, 1953.
7. Felder, D. A.: Analysis of a Method of Phlebography of the Lower Extremity in the Semierect Position, Radiology. In press.
8. Felder, D. A., and Murphy, T. O.: The Evaluation of a Method of Phlebography of the Lower Extremities, SURGERY **37**: 198, 1955.
9. Sgalitzer, M., Kollert, V., and Demel, R.: Kontrast Darstellung Der Venen Im Röntgenbilde, Klin. Wchnschr. **102**: 1659-1663, 1931.
10. Braune, C. W.: Das Venensystem des Menschlichen Körpers. 2 Lief. Die Venen des Fusses und Unterschenkels, Leipzig, 1889, Veit und Komp.
11. Williams, A. F.: The Formation of the Popliteal Vein, Surg., Gynec. & Obst. **97**: 769-772, 1953.
12. Edwards, E. A., and Robuck, J. D.: Applied Anatomy of the Femoral Veins and Its Tributaries, Surg., Gynec. & Obst. **85**: 547-557, 1947.

TREATMENT OF PENETRATING WOUNDS OF THE HEART: EXPERIMENTAL AND CLINICAL OBSERVATIONS*

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FOR centuries the management of cardiac wounds has challenged the judgment and technical skill of surgeons. As early as 1649 Riolanus[24] suggested use of pericardicentesis in such injuries, and in 1829 Larrey,[18] the noted French surgeon, treated a cardiac wound by pericardial aspiration. He also conducted animal experiments to determine the cause of death in cardiac wounds. In 1886 Fischer[14] reported 452 cases of cardiac wounds treated by venesection and pericardial aspiration with a case fatality rate of 84 per cent. In 1895 Del Vecchio[10] demonstrated the feasibility of cardiorrhaphy in dogs. He also suggested the usefulness of pericardicentesis in the conservative management of wounds of the heart. Near the end of the nineteenth century several unsuccessful attempts were made to repair cardiac lacerations in patients, and to Rehn,[23] in 1896, goes credit for performing the first clinically successful cardiorrhaphy, which perhaps opened the way for the development of cardiac surgery.

Until the past decade emergency cardiorrhaphy was generally considered the treatment of choice in cardiac wounds, and in this country a number of surgeons, notably Elkin,[12] Bigger,[3] and Griswold,[15] accumulated wide experience with this method of treatment. However, even they reported a high mortality rate, and the operative mortality rate in this country was 50 per cent.[3] Recently, Griswold and Drye[16] reported twenty years' experience at the Louisville General Hospital totaling 108 cases of cardiac wounds with a mortality rate of 37.9 per cent. The mortality rate was reduced from 46 per cent in the early period (1933-1941) to 31.5 per cent for the later period (1941-1953). They recommended operation and cardiorrhaphy in almost all cardiac injuries, and during these respective periods the operability rate increased from 60 per cent to 89.5 per cent. Maynard and associates[19] collected eighty-one cases of penetrating cardiac wounds at Harlem Hospital with a gross mortality of 57 per cent. Among the sixty-one patients operated upon, the mortality was 42.7 per cent. Despite this high mortality they continued to advocate operative management as treatment of choice for cardiac wounds and recommended nonoperative treatment only for the mildest cases. They did not consider pericardicentesis as definitive treatment in cardiac injuries.

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Although pericardicentesis was employed by others previously, the rationale of this method together with fluid and blood replacement as definitive treatment in cardiac injuries was first recommended by Blalock and Ravitch[6] eleven years ago. Among the eighteen patients in their series treated in this manner, there was only one death. Elkin,[13] a former proponent of operative therapy in cardiac wounds, recently reported seventeen cases of patients treated conservatively with one death. Although conservative management of cardiac injuries results in a significantly higher incidence of survival, the advocates of this method of therapy agree that an occasional desperately ill patient who does not respond to conservative measures must undergo operation and attempted cardiorrhaphy.

In order to evaluate the operative and nonoperative treatment of penetrating wounds of the heart and pericardial tamponade, a series of experiments was performed to determine the factors influencing survival under these circumstances. The results of these experiments, together with an analysis of fifty-seven cases of patients with penetrating wounds of the heart admitted to Jefferson Davis Hospital during the past four years, form the basis of this report.

EXPERIMENTAL OBSERVATIONS

More than 100 adult mongrel dogs were used in these experiments. The dogs were anesthetized with morphine and pentobarbital or ether, and an intratracheal catheter was inserted. Whenever the experiment necessitated opening the chest, the lungs were artificially insufflated with air. The arterial and venous pressure, intrapericardial pressure, and intrapleural pressure were recorded.

A. *Experimental Cardiac Tamponade.*—Tamponade was induced in the anesthetized animal by instilling saline solution in 20 to 25 c.c. increments into the pericardial sac. In most instances a critical level of pericardial pressure was determined at ± 20 cm. saline solution, at which point blood pressure dropped to a mean of 25 to 40 mm. Hg. At this stage venous pressure (VP) exceeded pericardial pressure (PP) by 2.0 cm., a gradient which was apparently necessary for cardiac filling to occur at all. If pericardial pressure was slightly raised above this critical level, the VP and PP were almost equalized, arterial pressure declined sharply, and cardiac action ceased unless the pericardial pressure was released.[8] This, of course, demonstrated the resuscitative effect of pericardicentesis in cardiac tamponade and revealed quite strikingly that volumes of aspirant of as little as 5 to 10 c.c. had immediate influence upon recovery of circulation.

In the past the rationale of administration of infusions to patients with pericardial tamponade has been questioned because it was postulated that to raise venous pressure further in pericardial tamponade would be harmful. Elevating the venous pressure under these circumstances increases the right atrial pressure and pericardial pressure. This, in turn, further increases the

constricting effect on the vena cava and impairs cardiac filling. However, Cooper, Stead, and Warren[9] have clearly demonstrated that rapid continuous infusions of saline solution enabled the animal to withstand 92 to 146 per cent greater pericardial pressure. The present experiments revealed that rapid injections of approximately 300 c.c. of saline solution produced a slight but exceedingly transient rise in blood pressure, as already shown by Beck[4] and Sawyer.[25] Continuous massive infusions of saline solution had a somewhat more prolonged beneficial effect, but this, too, was soon dissipated unless pericardial pressure was released. Continuous blood transfusion produced a favorable effect in the presence of tamponade, roughly similar to the effect of continuous saline infusion. These results, therefore, are in agreement with those of Cooper and associates[9] in that further increase in venous pressure by means of infusions in the presence of pericardial tamponade apparently enhances cardiac filling in spite of the associated elevation of pericardial pressure which is produced.[8]

Circulatory stimulants in dilute continuous infusions were tried in the presence of tamponade. The vasoconstrictor drug, norepinephrine, proved particularly effective in raising systemic blood pressure, even in the presence of tamponade. This elevation of blood pressure occurred in spite of an associated increase in VP and an increase of pericardial pressure sometimes two to three times greater than the critical level. Studies were also undertaken to determine whether the increased blood pressure represented actual increase in cardiac output or was simply a manifestation of the peripheral vasoconstrictor effect. The vasoconstrictor effect appeared to be the most significant one. Nevertheless, animals in critical condition could be resuscitated by this drug, and it appears to have clinical usefulness as an adjunct to therapy. Warren[27] reported that high normal peripheral resistance occurs regularly in the presence of cardiac tamponade, and on the basis of our experiments it appears that further increase in peripheral resistance may exert a temporarily beneficial effect upon the circulation.

A study was made of the effect of elevated blood alcohol upon the ability of the animal to withstand cardiac tamponade. Alcohol was administered intravenously to the animal until a level of intoxication was reached. Alcohol, which is a central nervous system depressant and peripheral vasodilator, significantly decreased the animals' tolerance to cardiac tamponade and furthermore interfered with the usual resuscitative effects of norepinephrine.[8]

The effect of artificial pulmonary insufflation upon circulation in pericardial tamponade was evaluated in order to explain the frequency with which sudden circulatory failure may occur during the initial phase of positive pressure anesthesia. Experimentally alternating positive pressure insufflation of the lung produced further increase in PP and VP, leading to further fall in systemic pressure and frequently death. On the other hand, alternating positive-negative pressure insufflation was tolerated much better, and the negative phase appeared to enhance cardiac filling significantly.[8] From these studies it would appear that the type of pulmonary insufflation usually employed in

thoracic operations could be dangerous in the patient with tamponade and that death may ensue immediately upon introduction of the intratracheal tube and commencement of positive pressure anesthesia.

Experiments comparing the use of pentobarbital and ether as anesthetic agents in the presence of tamponade revealed that barbiturates reduced the tolerance for positive pressure anesthesia. These observations are in agreement with those of other workers,[5, 21] who have demonstrated the adverse effects of the barbiturates in positive pressure anesthesia.

B. *Experimental Cardiac Wounds.*—Experiments were conducted to determine the factors influencing survival in actual cardiac wounds in order to study the effect of the myocardial damage itself upon circulation. In order to evaluate these factors experimentally, it was necessary to construct an instrument which would inflict a cardiac wound of standard size and shape. An instrument was finally designed which made an incision by means of expandible blades as it was being withdrawn from the cardiac chamber.[7] Approximately 30 per cent of the animals wounded in this manner died and 80 per cent of these within the first thirty minutes. The majority of the dogs surviving the critical immediate period but dying in the next few hours presumably could have been saved by resuscitative measures. This suggests that patients who arrive at the hospital alive at least thirty minutes after injury have a type of cardiac wound that provides a reasonably good chance for survival. These observations would seem to support the advocacy of the nonoperative management of penetrating wounds of the heart.

Results of experiments related to the influence of location of the wound to survival indicated that left ventricular wounds of standard size caused a higher incidence of immediate fatality and tended to bleed more actively than comparable right-sided wounds. They also produced cardiac tamponade more frequently than wounds of the auricles. Lacerations to coronary vessels, particularly the anterior descending branch of the left coronary, were the most serious.

CLINICAL EXPERIENCE

Since Jan. 1, 1951, the surgical staff at Jefferson Davis Hospital has treated penetrating wounds of the heart by nonoperative means as the method of choice. Between Jan. 1, 1951, and Oct. 31, 1954, fifty-seven patients were admitted to the emergency ward with penetrating wounds of the heart. This included all patients admitted with any sign of life whatsoever, although some died immediately after admission and before any method of treatment could be instituted. Thus, among the fifteen patients in whom pericardicentesis was not performed, five died in less than ten minutes after arrival at the hospital.

Patients admitted to the hospital with stab wounds of the chest and precordium are examined promptly for signs of pericardial tamponade. Pericardicentesis is performed immediately, usually parasternally through a left fifth intercostal space, and blood is evacuated into a basin, where it is examined for clotting. If the blood is incoagulable, then it is assumed to be

from the pericardial sac, whereas if a coagulum forms, the blood may have been withdrawn from a cardiac chamber. Pericardial aspiration may be performed repeatedly, particularly wherever signs of recurring tamponade appear. The blood lost is replaced by blood transfusion, and while the blood is being crossmatched, infusions of glucose solution containing norepinephrine may be administered cautiously to raise blood pressure above 80 mm. mercury if possible. If, under careful observation and after several pericardicenteses, the condition of the patient worsens, thoracotomy is undertaken for attempted cardiorrhaphy. Thus, almost all patients with penetrating wounds of the heart, except those with relatively mild wounds, those who die soon after admission, or those in whom the diagnosis was not made, are treated by nonoperative means.

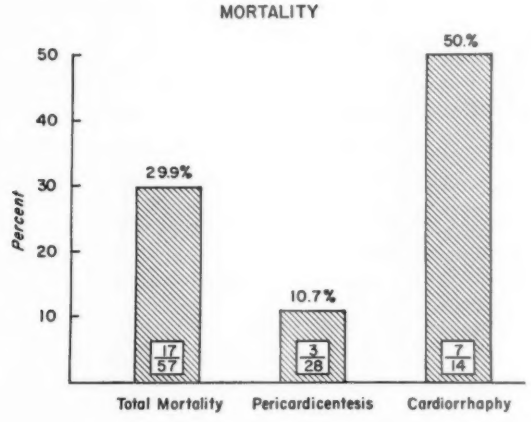

Fig. 1.—Penetrating wounds of the heart.

Among the fifty-seven patients with cardiac wounds, twenty-eight (49.1 per cent) were treated by nonoperative means alone (Table I), and in fourteen (24.6 per cent) cardiorraphy was attempted. Approximately 30 per cent of the fifty-seven patients died. The mortality rate of the group treated by operative means was five times that of the nonoperative group (Fig. 1). It is true that the patients treated surgically were the ones with the most severe injuries requiring more aggressive measures. On the other hand, among the seven survivors in the operative group were four patients in whom thoracotomy revealed that exploration was unnecessary because the laceration had sealed off completely. Comparison of operative with nonoperative methods of treatment usually raises the question of whether or not patients treated without exploration actually had a penetrating cardiac wound in the first place. In all patients included in the nonoperative group, however, the diagnosis of penetrating injury to the heart was based upon characteristic clinical manifestation and particularly the presence of incoagulable blood on pericardial aspiration. In most instances electrocardiograms were made and were helpful if evidence of myocardial injury was revealed. In spite of the objections which may be raised to the method of selection of patients for comparison, the striking difference in mortality cannot be disregarded.

TABLE I. MORTALITY RATE IN FIFTY-SEVEN CASES OF PENETRATING WOUNDS OF THE HEART ACCORDING TO METHOD OF TREATMENT

	NO. CASES	PER CENT	DEATHS	
			NUMBER	PER CENT
Pericardicentesis	28	49.1	3	10.7
Cardiorrhaphy	14	24.6	7	50.0
No treatment	15	26.3	7	46.7
Total	57	100.0	17	29.9

Fifty-two patients had lacerations or stab wounds of the heart, and five had gunshot wounds. Sixteen of the former and one of the latter group died. Presumably, most patients injured by gunfire who survive long enough to reach the hospital alive have relatively mild or grazing wounds inflicted by small-caliber weapons.

Complications in the nonoperative cases have not been serious. Three patients had persistent pericardial effusion lasting two to three weeks, which finally subsided spontaneously. None of the patients developed chronic constrictive pericarditis, although one patient treated by nonoperative means has had persistent, asymptomatic, mildly elevated venous pressure (160 mm. saline solution) two years later. Whereas pericardiectomy has been performed for posttraumatic chronic constrictive pericarditis in reported cases,[1, 2, 11, 20, 26] it does not appear to be a sufficiently frequent complication to contraindicate nonoperative management of cardiac wounds.

DISCUSSION

The results of nonoperative treatment, particularly in patients in this series treated by pericardial aspiration and blood transfusion, appear to justify continuance of this method of treatment. Furthermore, a number of factors exist in most general hospitals which may render impractical routine exploratory thoracotomy and repair of the laceration. Such heroic surgical maneuvers require skilled personnel to prepare the operating room, give the anesthetic, and perform the operation. Such personnel are not always available. Moreover, such injuries tend to appear on the busiest nights in the emergency room, and occasionally two patients with the same type of wound are admitted simultaneously. Thus, fortunately, not only is conservative management of penetrating wounds more convenient for the hospital personnel but, more importantly, it appears to offer the patient the best possible chance for survival in most instances. Another important advantage of this method lies in its value in temporarily resuscitating even the most desperate cases and thus maintaining life until cardiorrhaphy could be performed should this prove necessary. Accordingly, we are in complete agreement with Ravitch and Blalock[22] and Elkin[13] in recommending that initial treatment of penetrating wounds of the heart should consist of nonoperative methods and that attempted cardiorrhaphy should be reserved for those patients whose response to this method of therapy is not maintained.

SUMMARY

1. Experimental and clinical observations are presented to support the advocacy of nonoperative treatment of cardiac wounds.

2. In experimental pericardial tamponade relatively small reduction in volume of pericardial fluid produces an immediate and strikingly favorable influence upon circulation. The vasoconstrictor drug, norepinephrine, also proved to have a favorable effect upon circulation through elevation of systemic blood pressure. On the other hand, alternating positive pressure insufflation of the lungs in the presence of pericardial tamponade produced an unfavorable effect upon circulation.

3. A standard type of cardiac injury was produced experimentally and revealed that death following such an injury occurred within the first thirty minutes in the majority of animals.

4. An analysis is presented of a series of fifty-seven patients with penetrating wounds of the heart between Jan. 1, 1951, and Oct. 31, 1954, during which period nonoperative management was used as the method of choice. Fifteen of the patients received no treatment with a mortality of 46.7 per cent. Among the remainder, fourteen were treated by exploratory thoracotomy and attempted cardiorrhaphy with a mortality of 50 per cent, and twenty-eight by nonoperative therapy with a mortality of 10.7 per cent.

5. On the basis of these observations nonoperative management is recommended in all cases either as specific therapy or as preparatory measure to emergency thoracotomy in those patients in whom response to this method of treatment is not maintained.

REFERENCES

1. Ada, A. E. W., Jones, O. R., and Sheenan, A. D.: Partial Pericardiectomy in a Case of Hemopericardium Due to Nonpenetrating Trauma, J. Thoracic Surg. **20**: 105, 1950.
2. Barker, P. S., and Johnston, F. D.: Chronic Pericarditis With Effusion, Circulation **2**: 134, 1950.
3. Bigger, I. A.: Heart Wounds, J. Thoracic Surg. **8**: 239, 1939.
4. Beck, C. S.: Further Observations on Stab Wounds of the Heart, Ann. Surg. **115**: 698 (April) 1942.
5. Beecher, H. K., and Moyer, C. A.: Mechanism of Respiratory Failure Under Barbiturate Anesthesia (Evipal, Pentothal), J. Clin. Invest. **20**: 549, 1941.
6. Blalock, A., and Ravitch, M. M.: A Consideration of the Nonoperative Treatment of Cardiac Tamponade Resulting From Wounds of the Heart, SURGERY **14**: 157, 1943.
7. Brockman, H. L., Cooley, D. A., and DeBakey, M. E.: Factors Influencing Survival in Experimental Heart Wounds, Proc. Surg. Forum, Clin. Congress Am. Coll. Surgeons, Chicago, October, 1953, Philadelphia, 1954, W. B. Saunders Company, p. 108.
8. Cooley, D. A., and Brockman, H. L.: Factors Influencing Survival in Experimental Cardiac Tamponade, Proc. Surg. Forum, Clin. Congress Am. Coll. Surgeons, New York, September, 1952, Philadelphia, 1953, W. B. Saunders Company, p. 264.
9. Cooper, F. W., Jr., Stead, E. A., Jr., and Warren, J. V.: The Beneficial Effect of Intravenous Infusions in Acute Pericardial Tamponade, Ann. Surg. **120**: 822, 1944.
10. Del Vecchio: Sutura del cuore, Rifirma med. **79**: 1895, cited by Ballance, C.: The Surgery of the Heart, Lancet **1**: 1, 73, 134, 1920.
11. Ehrenhaft, J. L., and Taber, R. E.: Hemopericardium and Constrictive Pericarditis, J. Thoracic Surg. **24**: 355 (Oct.) 1952.
12. Elkin, D. C.: Wounds of the Heart, Ann. Surg. **120**: 817 (Dec.) 1944.
13. Elkin, D. C., and Campbell, R. E.: Cardiac Tamponade: Treatment by Aspiration, Ann. Surg. **133**: 623, 1951.
14. Fischer, Georg: Langenbeck's Arch. **9**: 608, 1886, cited by Ballance, see Ref. 10.

15. Griswold, R. E., and Maguire, C. H.: Penetrating Wounds of the Heart and Pericardium, Surg., Gynec. & Obst. **74:** 406 (Feb.) 1942.
16. Griswold, R. A., and Drye, J. C.: Cardiac Wounds, Ann. Surg. **139:** 783-785 (June) 1954.
17. Johns, T. N. P., discussion of Elkin.[13]
18. Larrey, D. J.: Clin. chir. **2:** 303, 1829, cited by Ballance, see Ref. 10.
19. Maynard, A. DeL., Cordice, J. W. V., Jr., and Naclerio, E. A.: Penetrating Wounds of Heart, a Report of 81 Cases, Surg., Gynec. & Obst. **94:** 605, 1952.
20. Overholt, R. H., Burwell, C. S., Woodbury, J. W., and Walker, J. H.: Constrictive Pericarditis and Constrictive Pleuritis Treated by Pericardiectomy and Pulmonary Decortication, J. Thoracic Surg. **23:** 1, 1952.
21. Price, H. L., Conner, E. K., Elder, J. D., and Dripps, R. D.: Effect of Sodium Thiopental on Circulatory Response to Positive Pressure Inflation of the Lung, J. Appl. Physiol. **4:** 629 (Feb.) 1952.
22. Ravitch, M. M., and Blalock, A.: Aspiration of Blood From Pericardium in Treatment of Acute Cardiac Tamponade After Injury: Further Experience With Report of Cases, Arch. Surg. **58:** 463, 1949.
23. Rehn, L.: Ueber penetrirende Herzwunden und Herzvalt, Arch. klin. Chir. **55:** 315, 1897.
24. Riolanus: Langenbeck's Arch. **9:** 608, 1886, cited by Ballance, see Ref. 10.
25. Sawyer, C. G., Johnston, F. R., and Lambeth, W. A.: Factors in Acute Cardiac Tamponade: An Altered Concept, Proc. Surg. Forum, Clin. Congress Am. Coll. Surgeons, San Francisco, November, 1951, Philadelphia, 1952, W. B. Saunders Company, p. 282.
26. Skinner, H. L., and Farr, K. F.: Decortication of Heart, Report of a Case, J. A. M. A. **152:** 234, 1953.
27. Warren, J. V., Brannon, E. S., Stead, E. A., and Merrill, A. J.: Pericardial Tamponade From Stab Wound of the Heart and Pericardial Effusion or Empyema: A Study Utilizing the Method of Right Heart Catheterization, Am. Heart J. **31:** 418-425, **1946.**

STUDIES IN CORONARY OCCLUSION WITH PARTICULAR REFERENCE TO THE LACK OF EFFECT OF EXPERIMENTALLY PRODUCED MYOCARDIAL INFARCTION UPON EXERCISE TOLERANCE

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THE clinical importance of coronary artery disease and myocardial infarction has prompted, during the past twenty years, a number of experimental studies aimed at the development of surgical techniques for increasing the circulation to the ischemic myocardium. Methods investigated have included grafting of omentum, skeletal muscle, and lung to the myocardium,[1-3] the production of adhesions between the pericardium and the heart,[4] ligation of the great cardiac vein,[5] implantation of the internal mammary artery into the heart wall,[6, 7] and arteriolization of the coronary sinus.[8]

The method most commonly used for evaluating the efficacy of these procedures has been measurement of the protection they afford the experimental animal subjected to coronary artery ligation. That careful control studies are essential in such experiments is apparent from the wide variation in mortality following ligation of the anterior descending branch of the left coronary artery. Miller[9] reported no deaths. Goldman,[10] who ligated the artery "at a relatively high level," had a 15 per cent mortality. Thompson[11] reported a 50 per cent mortality following ligation of the artery 1 cm. below its origin, and Vineberg,[12] who ligated the artery at its point of origin, noted a 90 per cent mortality. In the largest series reported, Hahn and Beck[13] found a 70 per cent mortality in 100 dogs subjected to ligation of the artery at its origin. Additional methods for evaluation of revascularization procedures have included microscopic studies, injection of the coronary system with plastic materials and clearance techniques, x-ray studies after injection of radiopaque material into the coronary arteries, study of the coronary circulation with fluorescein and radioactive erythrocytes,[14] motion pictures for recording the ballooning out of the infarcted segment, efforts to estimate the extent of infarction by epicardial electrocardiography,[10] and measurement of pressure in and flow from the distal end of the divided coronary artery.[15]

All these methods of study have in common the performance of a procedure designed to increase the collateral circulation, followed by coronary artery ligation. They have provided much useful information. There can be

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no doubt, for example, that carefully controlled mortality studies yield valuable data concerning the protection afforded by any given procedure against subsequent sudden interruption of arterial inflow into an important branch of the coronary artery. The clinical problem with which we are faced is, however, somewhat different. It concerns the possible usefulness of any proposed method in increasing the blood supply to the heart and alleviating cardiac dysfunction in the presence of well-established coronary artery disease and myocardial ischemia. For this reason it would be desirable if proposed methods of treatment could be evaluated in experimental animals following coronary artery ligation and the production of an infarct.

The principal object of this study was to learn whether dogs with such experimentally produced myocardial infarction have an objectively measurable decrease in exercise tolerance which would serve as a valid basis for evaluating the efficacy of procedures designed to bring about revascularization. Certainly limitation of capacity for physical activity is a striking feature of most cases of myocardial infarction and angina pectoris in man. This problem has received little attention in experimental works. O'Shaughnessy[1] ligated the left anterior branch in two greyhounds and three months later ran them on their "usual course." He reported that they were more distressed than usual by this activity. After cardio-omentopexy, however, one dog was found to perform normally. Vineberg[16] found that his control dogs could run from nine to twelve minutes on a horizontal treadmill at eight and one-half miles per hour. Three to four months after the left anterior descending branch was wrapped with cellophane so as to cause severe constriction, the dogs tolerated such running for only two to four minutes. Some of these animals were then subjected to implantation of the internal mammary artery into the myocardium. Subsequently these animals could run on the treadmill for from six to eight minutes, while no improvement was noted in the remainder. Burchell,[17] on the other hand, stated that there was little or no evidence of cardiac disability in animals which had survived ligation of the anterior descending or circumflex branch of the left coronary artery. He used a treadmill inclined twenty-five degrees and ran his dogs at 4.5 miles per hour. Constricting collars were placed on the three main coronary arteries in two operations so as to decrease the diameter of the vessels from 35 to 60 per cent. The animals which survived the first week apparently ran normally on the treadmill. In three dogs with their three main coronaries gradually but completely occluded, the exercise tolerance on the treadmill was again normal. These animals, however, did not show infarcts on post-mortem study. Some animals were subjected to acute ligation of coronary arteries and were later shown to have large scars of the myocardium. The author mentioned that they seemed to be capable of normal activity but did not state whether they had been tested on the treadmill.

METHOD OF STUDY

Thirty healthy mongrel dogs weighing between 10 and 20 kilograms were trained to run on a horizontal treadmill until they ran quite willingly and

without balking. Animals that would not cooperate were excluded from the study. Each dog was run at a uniform speed until he was obviously exhausted, and the speed of the treadmill and duration of the physical effort were recorded. Each of the dogs which survived coronary artery ligation was again run on the treadmill at the same speed one month after operation. The criteria for exhaustion included extreme tachypnea, cyanosis of the tongue, and obvious attempts to escape from the treadmill. It was obvious that this end point was not as sharp as might have been desired. It was felt, however, that comparative data were valid in view of the fact that only cooperative, trained animals were used and that all the training and testing were done by one individual.

The animals were operated upon under ether-oxygen anesthesia administered through an endotracheal tube by means of an intermittent insufflation apparatus following induction with intravenously administered thiopental sodium. Following left lateral thoracotomy the heart was exposed through the fourth intercostal space. The left atrial appendage was gently retracted by means of a stay suture placed through its tip, and the bifurcation of the left coronary artery was dissected free. The anterior descending branch was divided at its origin between two fine silk ligatures. The pericardium was sutured together, and the chest was closed in layers with interrupted silk sutures.

TABLE I. DATA CONCERNING ANIMALS WHICH DIED AFTER CORONARY ARTERY LIGATION

NUMBER OF ANIMAL	APPROXIMATE INTERVAL BETWEEN LIGATION AND DEATH	ORIGIN OF SEPTAL BRANCH FROM ANTERIOR DESCENDING ARTERY DISTAL TO POINT OF DIVISION
603	30 min.	No
604	24 hr.	No
607	24 hr.	No
609	30 min.	No
610	30 min.	No
612	30 min.	No
614	5 min.	No
620	12 hr.	No
622	24 hr.	Yes
625	9 hr.	Yes
628	4 days	Yes
631	24 hr.	No
634	3 min.	No
642	1 min.	No
658	24 hr.	Yes
660	24 hr.	No
662	24 hr.	Yes
668	10 days	No

Electrocardiographic studies were carried out pre- and postoperatively in a number of animals. All animals were subjected to post-mortem study. In each the location and extent of the infarct were noted and the proximal portion of the coronary artery was dissected free in order to verify the site of the ligation and to determine whether the septal branch arose from the an-

terior descending branch distal to the point of division. In some animals coronary artery injection studies with radiopaque material were performed. In others histologic studies of the infarcted areas were made.

RESULTS OF STUDY

Mortality.—Of the thirty dogs operated upon, eighteen died in from one minute to ten days after ligation, an over-all mortality of 60 per cent (Table I). Sixteen of the eighteen dogs that died did not live as long as twenty-four hours. All those that survived longer than ten days remained healthy. They were sacrificed from thirty-one to seventy-one days after operation.

Fig. 1.—Photograph of the anterior surface of a dog's heart one month after ligation and division of the anterior descending branch of the left coronary artery. The area of infarction can be seen to extend from just below the left auricle to the apex of the left ventricle. It involves the left ventricular wall for a distance of 2.5 cm. to the left of the interventricular septum.

Post-mortem studies demonstrated that the anterior descending branch had been divided at the point of origin in all animals. In five, however, the septal coronary artery arose anomalously from the anterior descending branch, and consequently circulation to this vessel was interrupted in these five exceptional cases. All five of these animals died. If these animals are excluded from consideration there remain twenty-five dogs with normal origin of the septal branch from the left main artery. Thirteen of these died, a mortality of 52 per cent.

A large infarct involving the anterior surface of the left ventricle was present in every animal (Figs. 1 and 2). No infarct was smaller than 2.5 by 4 cm. in size. Sections from the ischemic portion of the ventricular wall showed changes typical of myocardial infarction (Fig. 3). Roentgenograms of specimens in which the coronary ostia were injected by the technique of

Fig. 2.—Photograph of cross sections of dog's heart showing thinning of ventricular wall at site of infarction. *A*, A transverse slice of the center of the heart. The extreme thinning of the anterior wall of the left ventricle is noted. *B*, Cross sections near the apex. Thinning and scarring of the myocardium are seen to extend to the apex itself.

Schlesinger[18] outlined the entire coronary tree (Fig. 4), and demonstrated that the anterior descending branch had been severed at its point of origin and that the infarcted area had sparse blood supply compared with the remainder of the heart. They also showed that the left anterior descending branch remains patent and fills by retrograde flow through collateral channels.

TABLE II. EXERCISE TOLERANCE BEFORE AND AFTER CORONARY ARTERY LIGATION

NUMBER OF DOG	TIME ON TREADMILL			
	PREOPERATIVE		POSTOPERATIVE	
	SPEED IN M.P.H.	DURATION IN MINUTES	SPEED IN M.P.H.	DURATION IN MINUTES
608	3	80	3	65
615	4	75	4	65
617	4	85	4	90
621	5	40	5	35
635	4	25	4	28
638	6	45	6	42
639	4	50	4	56
650	4	45	4	40
651	6	20	6	17
661	6	25	6	28
666	9	23	9	20
667	9	26	9	28

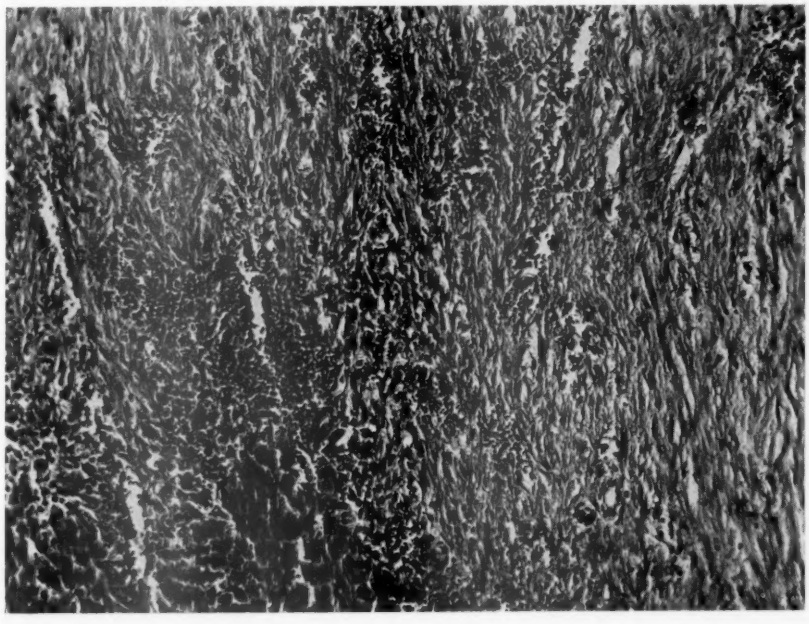


Fig. 3.—Photomicrograph of a section through the infarcted area showing replacement of heart muscle by fibrous tissue and considerable white-cell infiltration. This animal (668) died ten days after ligation.

Exercise Tolerance Studies.—The data concerning pre- and postoperative tolerance studies are presented in Table II. No significant difference was noted between the preoperative tolerance as measured by treadmill studies and that observed one month after ligation of the coronary artery. Seven dogs performed better before ligation, although the differences were rather

insignificant. The maximal difference noted was in Animal 608, whose capacity decreased 19 per cent. On the other hand, five animals performed slightly better during the postoperative test. The maximal increase was noted in Dog 639, the performance of which was 12 per cent better than in the preoperative test. Altogether it is apparent that no significant difference was noted between the tests carried out before operation and one month later.

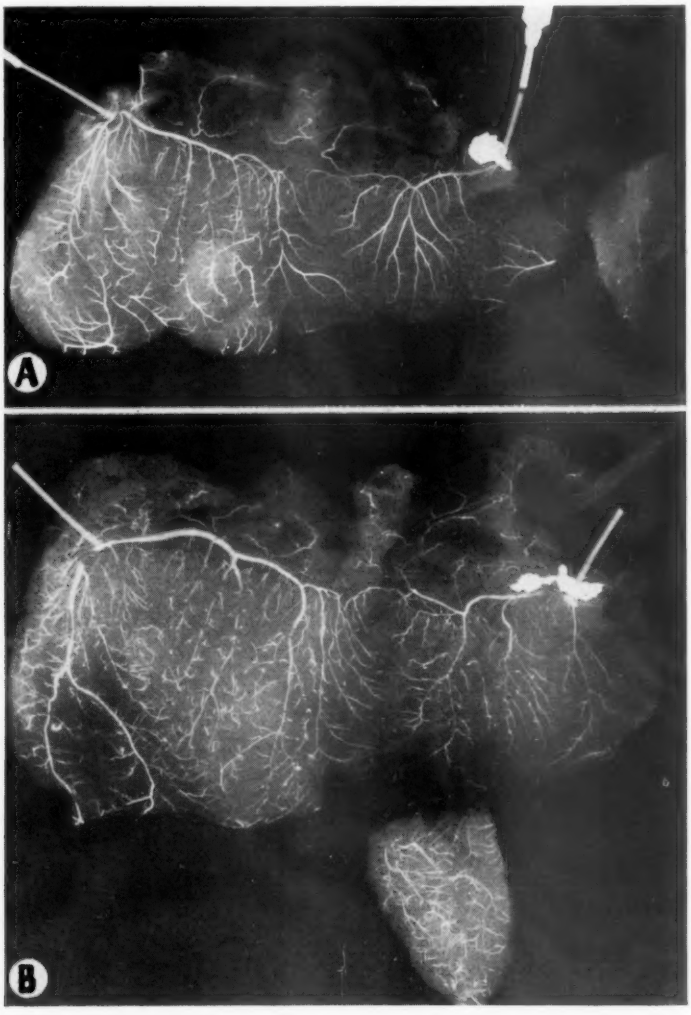


Fig. 4.—Radiograms of dog's heart injected and cut by technique of Schlesinger. *A*, Normal heart. The right coronary is easily seen on the right, while the circumflex and anterior descending branches of the left coronary are seen on the left. These injection studies do not show well the left main coronary artery or its septal branch. The septum is shown below. *B*, Injection studies one month after coronary ligation and division. Easily seen are the radiolucent area of the left ventricular wall, which represents the area of infarction, and the interruption of the anterior descending branch at its origin. Collateral communications to the distal branches of the anterior descending artery are seen arising mostly from branches of the circumflex artery.

Electrocardiographic Studies.—Four of the surviving dogs had preoperative and repeated postoperative electrocardiographic studies until they were exercised one month postligation. The control tracings were variable but

followed the pattern described by other investigators. The S-T segments were normal. The Q waves were small, except in one case where the Q wave was as deep as the R wave was tall. R waves were constantly present and tall in both standard and precordial leads. After occlusion of the anterior branch of the left coronary artery the S-T segment assumed its characteristic pattern of injury deflection in the standard and precordial leads but returned to isoelectric levels in the standard leads within twenty-four hours. In the left precordial leads S-T elevation persisted in two of the four dogs for as long as four weeks postoperatively. More significant, however, was the finding, in all four cases, of deep QS waves in Lead I and in the left precordial leads after the first day. These changes lasted at least four weeks (Fig. 5).

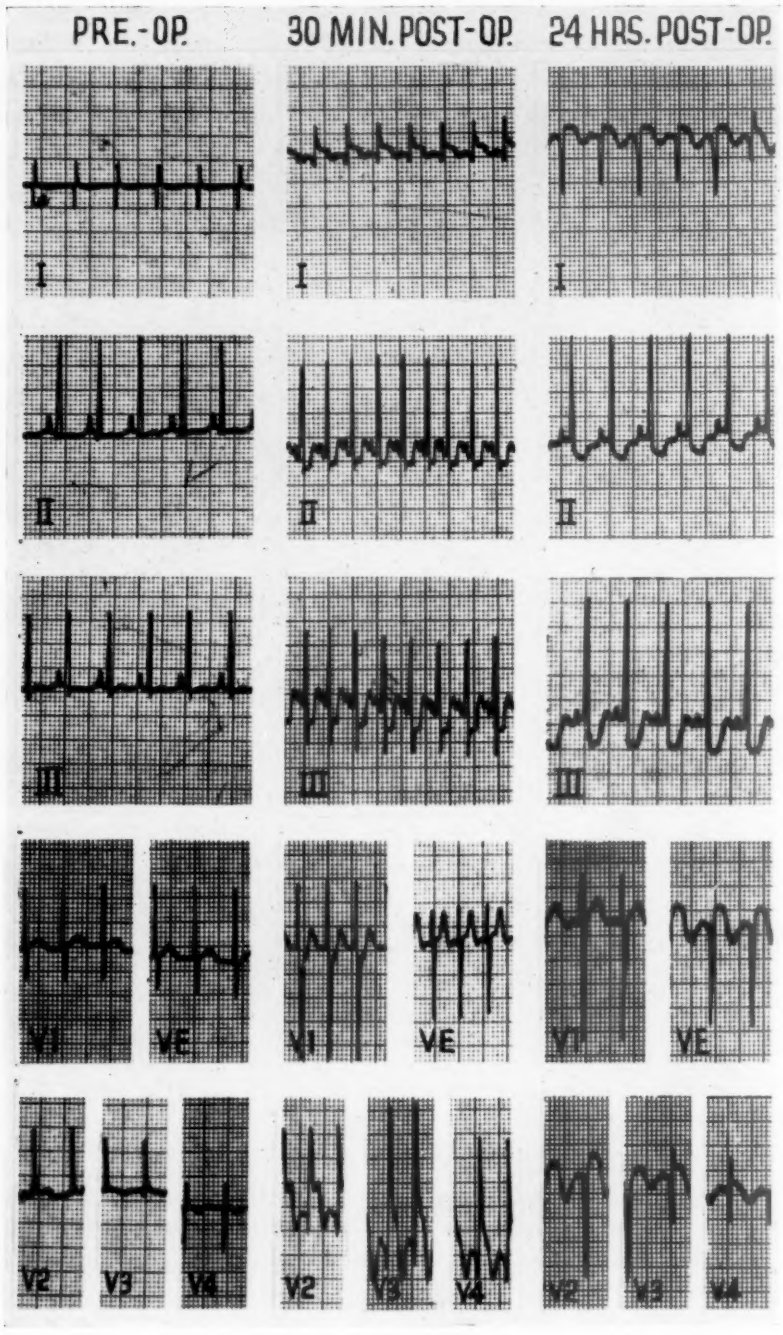
DISCUSSION

The mortality rate noted in this study was somewhat lower than that reported by some investigators and considerably higher than that reported by others. Eighteen of thirty dogs died, an over-all mortality of 60 per cent. Sixteen of the eighteen dogs that died did not survive as long as twenty-four hours. Vineberg[19] and Hahn and Beck[13] have emphasized the importance of the level of ligation of the anterior descending branch with regard to the mortality. In the dog, the interventricular septum receives its blood supply in large measure from a septal artery which normally arises from the left coronary artery near its point of bifurcation.[26] Occasionally the septal artery originates from the proximal portion of the anterior descending branch, and hence blood flow to this important vessel is interrupted by division of the anterior descending artery at its point of origin. This anomaly was noted in five of our thirty animals, and death occurred in all five. It is suggested that careful dissection, such as was done in this investigation, be carried out in all studies of this sort in order better to evaluate mortality figures. If the five animals with anomalous origin of the septal artery were eliminated from consideration, the mortality in the present study would be 52 per cent.

In all surviving animals post-mortem studies established the presence of a large anterior myocardial infarction. Whenever injection studies were carried out it was demonstrated that the anterior descending branch distal to the point of division remained patent through tiny collateral channels. Such retrograde circulation into this vessel, however, did not provide sufficient circulation to prevent massive infarction.

Electrocardiographic studies of dogs with myocardial infarcts have been conducted for some time, but the diagnostic electrocardiographic features of infarction with the usual leads have not been clearly outlined. This is especially true of long-term studies. Smith[21] placed great emphasis on T-wave changes and stated that all his dogs with anterior infarcts showed early, peaked T waves which became markedly negative in twenty-four hours and then slowly returned to normal in from two to four days. Other workers, however, reject T-wave changes as a diagnostic feature. Barnes[22] obtained

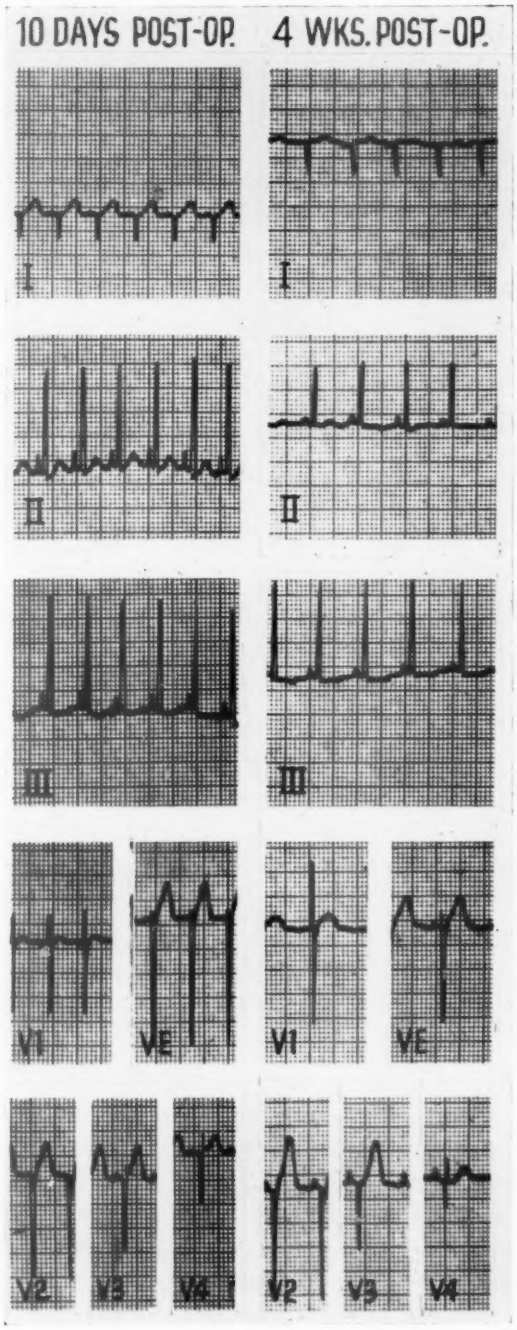
sharp, deep inversion of the T waves with incision of the pericardium and manipulation of the heart alone. Harris and Hussey[23] emphasized the extreme variability of the T waves in control animals, although Peterson[24] found that when he laid normal beagle dogs supine rather than on their side the T



A.

Fig. 5.—*A* and *B*, Electrocardiographic studies in dog with ligation and division of the anterior descending branch at its origin.

waves were no longer variable. Most workers noted the presence of a low-voltage R wave in Lead I, sometimes preceded by small Q waves, but although they found that this alteration persisted for weeks, did not regard it as a diagnostic feature.[21, 23] Wilson[25] stated that the R wave is often absent in



B.

Fig. 5*B*. *(For legend see opposite page.)*

Lead I in cases of large infarcts of the left ventricle. RS-T modification has been thought the most valuable sign of myocardial injury.[22, 23, 26, 27] This rarely occurs in normal dogs,[23] and manipulation of the heart without coronary occlusion does not affect the RS-T wave.[22] Unlike the other workers, Wood and Wolferth[27] did not find S-T deviations in the standard leads in coronary occlusion, but rather in the chest leads. These authors studied only the immediate effects of coronary occlusion. All authors who followed their animals for some time[22, 23, 26] found that these S-T changes reverted to normal in twenty-four hours. It is apparent from the literature that the only electrocardiographic findings on standard leads that persist twenty-four hours after coronary occlusion are the low-voltage R waves occasionally accompanied by Q waves in Lead I. These are not diagnostic features.

Epicardial leads have been used successfully by Wilson[28, 29] and Goldman[10] in dogs to demonstrate electrocardiographic evidence of long-term infarcts. When the lead was placed on the heart directly over a through-and-through infarct an intracavity type of deflection called a QS deflection was obtained. Wilson[28, 29] studied two dogs with precordial leads with infarction of the entire thickness of the left ventricular wall of more than one day's duration. One dog was subjected to ligation of the left anterior branch of the left coronary artery four days before. His left precordial leads showed the intracavity-type deflection found in the epicardial leads directly over the infarct and was considered to be characteristic of myocardial infarction. The other dog was similarly studied seventy-eight days after ligation of the same artery, and in this case the left precordial leads were not considered characteristic of myocardial infarction. Other studies of precordial leads in long-term experimental myocardial infarction were not found in the literature.

In the four animals in which repeated electrocardiographic alterations indicative of myocardial infarction were noted, the initial S-T segment changes which have been noted by others occurred regularly but disappeared within twenty-four hours. In addition, however, S-T segment elevation persisted in the left precordial leads for as long as four weeks after operation in two of four dogs. In all of them deep QS waves in Lead I and in the left precordial leads were observed after the first day and they lasted during the four weeks of observation.

It was disappointing to learn that no constant and significant decrease in exercise tolerance follows the experimental production of large myocardial infarcts. It had been hoped that a measurable exercise intolerance would accompany the presence of such infarcts. Had such proved to be the case one might have utilized measurements of this sort in testing the efficacy of various operative procedures aimed at myocardial revascularization. One might then have studied the potential value of such procedures when applied after, rather than before, coronary artery ligation. Even under such circumstances one would have failed to reproduce one essential feature of the problem in man, namely, the presence of disease in other portions of the coronary tree. Our

failure to demonstrate a decrease in exercise tolerance capacity in animals with established myocardial infarction and thus to provide a different approach for evaluation of procedures aimed at increasing myocardial circulation leaves us at the moment with the necessity for utilizing the conventional methods according to which coronary artery ligation is carried out after, rather than before, the corrective procedure itself. Even though these methods do not precisely simulate the situation in which they might be used in man, they do, nevertheless, provide valuable information concerning their effect upon myocardial circulation. In the final analysis the value of any proposed surgical aids must of necessity be established or refuted by carefully controlled observations in man.

REFERENCES

1. O'Shaughnessy, L.: An Experimental Method of Providing a Collateral Circulation to the Heart, Brit. J. Surg. **23**: 665, 1936.
2. Beck, C. S.: The Development of New Blood Supply to the Heart by Operation, Ann. Surg. **102**: 801, 1935.
3. Carter, B. N., Gall, E. A., and Wadsworth, C. L.: An Experimental Study of Collateral Coronary Circulation Produced by Cardiopneumonopexy, SURGERY **25**: 489, 1949.
4. Thompson, S. A.: Development of Cardio-pericardial Adhesions Following the Use of Talc, Proc. Soc. Exper. Biol. & Med. **40**: 260, 1939.
5. Fauteaux, M.: Experimental Study of the Surgical Treatment of Coronary Disease, Surg., Gynec. & Obst. **71**: 151, 1940.
6. Vineberg, A. M.: Development of an Anastomosis Between the Coronary Vessels and a Transplanted Internal Mammary Artery, Canad. M. A. J. **55**: 117, 1946.
7. Vineberg, A. M.: Treatment of Coronary Artery Insufficiency by Implantation of the Internal Mammary Artery Into the Left Ventricular Myocardium, J. Thoracic Surg. **23**: 42, 1952.
8. Beck, C. S., Stanton, E., Batuichok, W., and Leiter, E.: Revascularization of the Heart by Graft of a Systemic Artery Into the Coronary Sinus, J. A. M. A. **137**: 436, 1946.
9. Miller, J. L.: Effect on the Heart of Experimental Obstruction of the Left Coronary Artery, Arch. Int. Med. **3**: 467, 1909.
10. Goldman, A., Shaw, C., Corday, E., Fields, J., Kennamer, S. R., Smith, A., Lindgren, I., and Prinzmetal, M.: Experimental Methods for Detection of Changes of Blood Supply to the Heart, J. Thoracic Surg. **24**: 105, 1952.
11. Thompson, S. A.: An Operation for the Relief of Coronary Artery Disease, Quart. Bull., Sea View Hosp. **5**: 175, 1940.
12. Vineberg, A. M., and Niloff, P. H.: The Value of Surgical Treatment of Coronary Artery Occlusion by Implantation of the Internal Mammary Artery Into the Ventricular Myocardium, Surg., Gynec. & Obst. **91**: 551, 1950.
13. Hahn, R. S., and Beck, C. S.: Revascularization of the Heart, Circulation **5**: 801, 1952.
14. Prinzmetal, M., Bergman, H. C., Kruger, H. E., Schwartz, L. L., Simkin, B., and Sobin, S. S.: Studies on the Coronary Circulation. III. Collateral Circulation of Beating Human and Dog Hearts With Coronary Occlusion, Am. Heart J. **35**: 689, 1948.
15. Gregg, D. E., Thornton, J. J., and Mautz, F. B.: The Magnitude, Adequacy and Source of the Collateral Blood Flow and Pressure in Chronically Occluded Coronary Arteries, Am. J. Physiol. **127**: 161, 1939.
16. Vineberg, A. M., and Miller, D.: Functional Evaluation of Internal Mammary Coronary Artery Anastomosis, Am. Heart J. **45**: 873, 1953.
17. Burchell, H. R.: Adjustments in Coronary Circulation After Experimental Coronary Occlusion, Arch. Int. Med. **65**: 240, 1940.
18. Schlesinger, M. J.: An Injection Study of Coronary Artery Occlusions and Anastomoses, Am. Heart J. **15**: 528, 1938.
19. Vineberg, A. M., discussion of reference 8.
20. Moore, R. A.: The Coronary Arteries of the Dog, Am. Heart J. **5**: 743, 1930.
21. Smith, F. M.: The Ligation of Coronary Arteries With E.C.G. Study, Arch. Int. Med. **22**: 8, 1916.
22. Barnes, A. R., and Mann, F. C.: E.K.G. Changes Following Ligation of the Coronary Arteries of the Dog, Am. Heart J. **7**: 477, 1932.
23. Harris, B. R., and Hussey, R.: The E.K.G. Changes Following Coronary Artery Ligation in Dogs, Am. Heart J. **12**: 724, 1936.

24. Peterson, E. S., and Rickets, H. T.: Electrocardiogram of the Beagle Dog, Proc. Soc. Exper. Biol. & Med. 77: 330, 1951.
25. Wilson, F. N., Hill, I. G. W., and Johnston, F. D.: The Form of the Electrocardiogram in Experimental Myocardial Infarction. I. Septal Infarcts and the Origin of the Preliminary Deflections of the Canine Levocardiogram, Am. Heart J. 9: 596, 1934.
26. Gross, L., and Calef, B.: E.C.G. Changes in the Dog Following Sudden Occlusion of the Left Anterior Descending Coronary Branch and in Various Experimental Conditions, Am. Heart J. 14: 677, 1937.
27. Wood, F. C., and Wolferth, C. C.: Experimental Coronary Occlusion, Arch. Int. Med. 51: 771, 1933.
28. Wilson, F. N., Hill, I. G. W., and Johnston, F. D.: The Form of the Electrocardiogram in Experimental Myocardial Infarction. III. The Later Effects Produced by Ligation of the Anterior Descending Branch of the Left Coronary Artery, Am. Heart J. 10: 903, 1935.
29. Wilson, F. N., Johnston, F. D., and Hill, I. G. W.: The Form of the Electrocardiogram in Experimental Myocardial Infarction. IV. Additional Observations on the Later Effects Produced by Ligation of the Anterior Descending Branch of the Left Coronary Artery, Am. Heart J. 10: 1025, 1935.

BILE DRAINAGE AFTER CHOLEDOCHOSTOMY IN MAN, WITH SOME OBSERVATIONS ON BILIARY FISTULA*

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IN THIS paper we present measurements of the volumes of bile drained from a choledochostomy in man. Although the secretion of bile has frequently been studied in the experimental animal, we have not been able to find reference to any systematic observations on human bile flow.

In their classical experimental studies, McMaster, Broun, and Rous[1] (1923) established biliary fistulas in dogs and observed the effect of the operation and of exercise, hot weather, the relief of obstruction, and other normal and pathologic influences on the total daily bile flow. It is possible to keep a bile fistula dog in normal health for months or years if careful attention is paid to the diet (Hawkins and Whipple,[2] 1935 and 1938). Such bile fistula dogs have been used in quantitative studies of the effect of cholagogues and of the relationship between hemoglobin breakdown and bile pigment excretion.

With[3] (1945) collected data on bilirubin concentration of the bile and the daily bilirubin output in man. In nineteen of his thirty-five patients the data are satisfactorily for calculating the volume of bile drained, and the results are considered with our own.

METHODS

Data were collected after twenty-seven operations for choledochostomy, involving twenty-five patients (two having two operations). The diagnoses were cholelithiasis in twenty, hepatic cirrhosis in two, carcinoma of the pancreas in two, and chronic pancreatitis in one. Before their operations, many of the patients suffered from varying degrees of jaundice, cholangitis, and liver damage or dysfunction.

Only one patient, suffering from cirrhosis, was left with a normal gall bladder during the period of drainage. In all the others it was removed at surgery or was so involved in carcinoma or inflammatory fibrosis as to be functionless. Thus the volumes of bile drained directly correspond with hepatic secretion. The factors of concentration in, and emptying of, the gall bladder can be eliminated.

Toward the end of operation in each case the bile duct was drained. In twelve of the operations a latex rubber T tube was used; in fifteen others a

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cuffed (Foley) catheter was passed up toward the porta hepatis. Inflation of the cuff ensured that all the bile formed drained externally. It was collected in a graduated bottle beneath the patient's bed and measured in six-hour periods. In all of With's[3] (1945) patients T-tube drainage of the common duct was used.

Drainage of the common duct after choledochostomy is widely accepted practice. It is not our purpose to discuss here the pros and cons of common duct drainage, but it may be emphasized that, by and large, strictures of the common duct come not from the irritation of T-shaped or other drainage tubes but from surgical mishaps.

In draining the common duct it is important to suture the side opening in its wall snugly round the drainage tube; otherwise leakage and loss of bile into the peritoneum or dressings will result. Further, a redundant loop of tube should be left inside the abdomen to prevent undue traction on it when the abdominal parietes contract, as in coughing after operation. Neglect of this precaution may result in the tube being pulled out from the duct.

RESULTS

Average Bile Loss After Choledochostomy.—Fig. 1 shows the data from the twenty-seven patients. Each point represents the average volume from eleven or more patients on the postoperative day concerned. The curve begins at about 250 c.c. daily and rises gradually to about 500 c.c., fifteen days after operation. The twenty-four-hour drainage ranged from 20 to 1,060 c.c. The average volume from the tenth day onward, when the flow leveled off, was 478 ± 186 c.c. per twenty-four hours. In some patients observations were continued for four to five weeks, but the number of data available on any one day fell off rapidly after the fifteenth day and therefore the "average" curve was discontinued at this point. However, the available figures suggest that the general level of flow remains sensibly unchanged afterward.

A moment's reflection will tell us that the true volume of bile secreted in health cannot be measured. In fact the bile normally mixes with the food. Also, its secretion is stimulated by the cholagogic action of the bile salts absorbed from the gut into the enterohepatic circulation. In our patients the bile drained externally. Thus the important enterohepatic circulation was interrupted. Also, all the patients had some disease of the biliary tree or liver before operation, and complete recovery during the relatively short period of drainage could not usually be expected. On the other hand, the irritant effect of the tube in the common duct and of the low-grade infection constantly associated with its presence may tend to increase the flow. Thus the average figure of 478 ± 186 c.c. can only approximate roughly the true normal daily bile flow in man.

Long-term physiologic experiments were not possible in these patients. However, we were able to compare the volume of bile drained 6 A.M.—6 P.M.

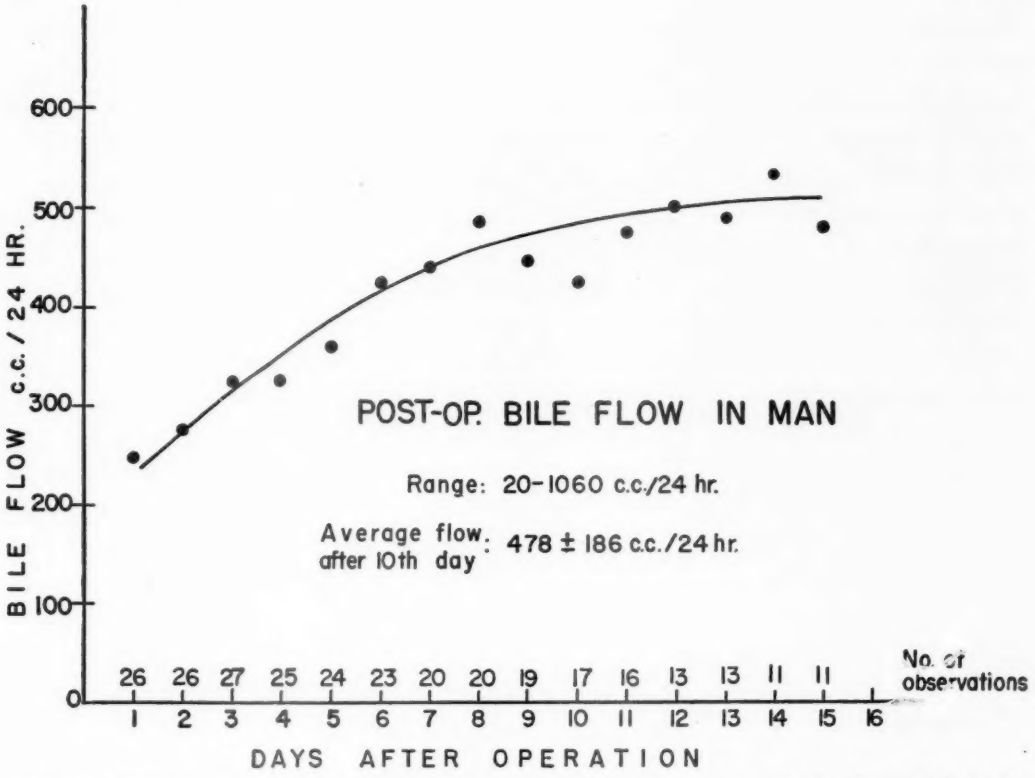
BILE FLOW c.c. / 24 HR.
600
500
400
300
200
100
0
POST-OP. BILE FLOW IN MAN
Range: 20-1060 c.c./24 hr.
Average flow, after 10th day: 478 ± 186 c.c./24 hr.
26 26 27 25 24 23 20 20 19 17 16 13 13 11 11
No. of observations
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
DAYS AFTER OPERATION

Fig. 1.—Average daily bile flow following choledochostomy in man. Each black disk is the average volume drained in the twenty-four-hour period concerned.

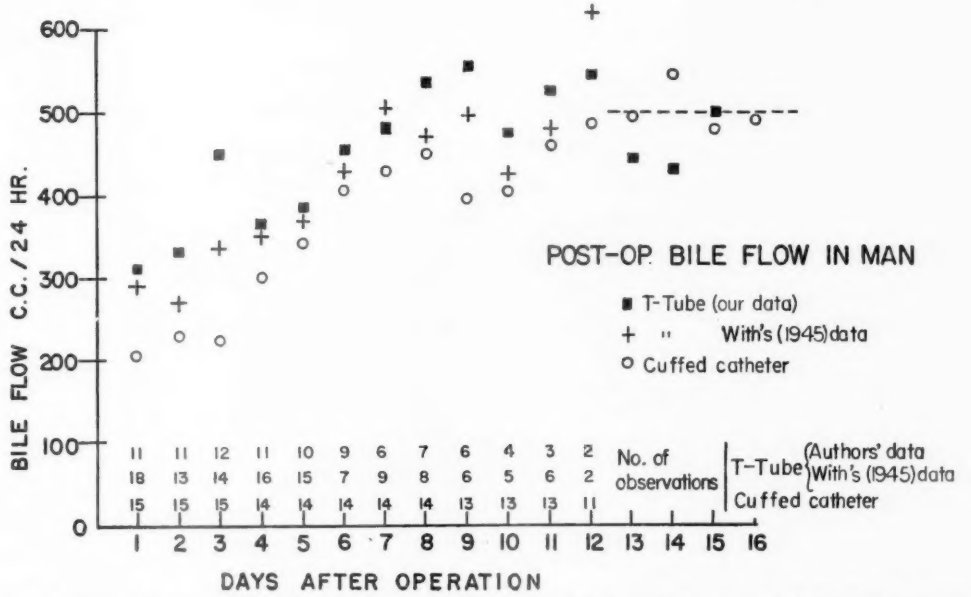
BILE FLOW C.C. / 24 HR.
600
500
400
300
200
100
0
POST-OP. BILE FLOW IN MAN
T-Tube (our data)
" With's (1945) data
Cuffed catheter
11 11 12 11 10 9 6 7 6 4 3 2
18 13 14 16 15 7 9 8 6 5 6 2
15 15 15 14 14 14 14 14 13 13 13 11
No. of observations
T-Tube (Authors' data / With's (1945) data)
Cuffed catheter
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
DAYS AFTER OPERATION

Fig. 2.—Comparison of bile drained via a T tube and a cuffed catheter inserted in the common bile duct following choledochostomy in man.

with the volume drained 6 P.M.—6 A.M. in twenty-one patients (327 pairs of observations), the respective means being 216 c.c. and 222 c.c. with large standard deviations.

Thus no evidence was obtained that the diurnal secretion of bile was greater than the nocturnal secretion. Of course, with contraction of the gall bladder after meals, the flow of bile into the duodenum will increase greatly, but our data suggest that in man the liver must secrete bile at virtually constant rate. No observations have been made on the effect of reintroducing bile into the alimentary tract, the ingestion of food of various types, or of cholagogic drugs on bile flow.

Comparison of Losses Through Cuffed Catheter and T Tube.—Fig. 2 compares the bile collected using a T tube in the common duct on the one hand and a cuffed catheter on the other. There was no selection of patients for the two types of drainage, except that some narrow ducts would not accommodate a cuffed catheter but would take a T tube. Hence there might have been bias toward using T tubes with undilated ducts. A priori it might be supposed that passage of bile through and round the horizontal limb of a T tube would allow appreciable quantities of bile to escape into the duodenum. However, our data show that the average drainage from a T tube is not less than that from a cuffed catheter. This result is surprising but is supported by With's[3] (1945) findings, which have also been plotted in Fig. 2.

It seems probable, therefore, that if the vertical limb of a T tube is kept patent, the pressure within the bile passages does not rise sufficiently to overcome the natural tone of the sphincter of Oddi. Thus virtually all the bile formed drains externally.

The completeness or otherwise of external biliary drainage may be ascertained by estimating the bilirubin content in material aspirated via a tube whose tip is in the second part of the duodenum or by analyzing the feces for urobilin. Sixteen twenty-four-hour specimens of duodenal aspirate have been analyzed from four patients with T-tube drains in the common duct. Bilirubin was absent from twelve and present in negligible concentration (less than 0.6 mg. per cent) in the remaining four. Of course, kinking or blocking of the vertical limb of the T tube may quickly result in loss of bile into the duodenum.

Drainage From a Biliary Fistula.—Just as an unimpeded T tube drains virtually all the bile being formed, so almost total loss of bile will occur from a fistula provided the track is widely patent. Moreover, even when virtually total drainage persists for long periods, a residual calculus or other obstruction at the lower end of the duct need not be postulated.

For example, the patient whose data are shown in Fig. 3 lost all his bile through a tube or fistula for nine weeks. At a first operation the gall bladder had been excised and a few small stones had been removed from the common

duct. He drained bile copiously afterward and developed severe constitutional symptoms from electrolyte deficiency. The cause of his deterioration was misapprehended and a second operation was thought necessary. The common duct was therefore re-explored and a drain was inserted. This was removed on the tenth day. In the meantime his electrolyte upset had been recognized and corrected. But bile in amounts 500 to 600 c.c. daily continued to be lost through the wound. He was then transferred to our Unit for treatment of the fistula. No satisfactory cholangiogram could be made along the track but, as shown in Fig. 3, the fistula suddenly closed thirty-two days after removal of the drain. Follow-up eighteen months later showed that it had remained healed and that the patient was enjoying excellent health.

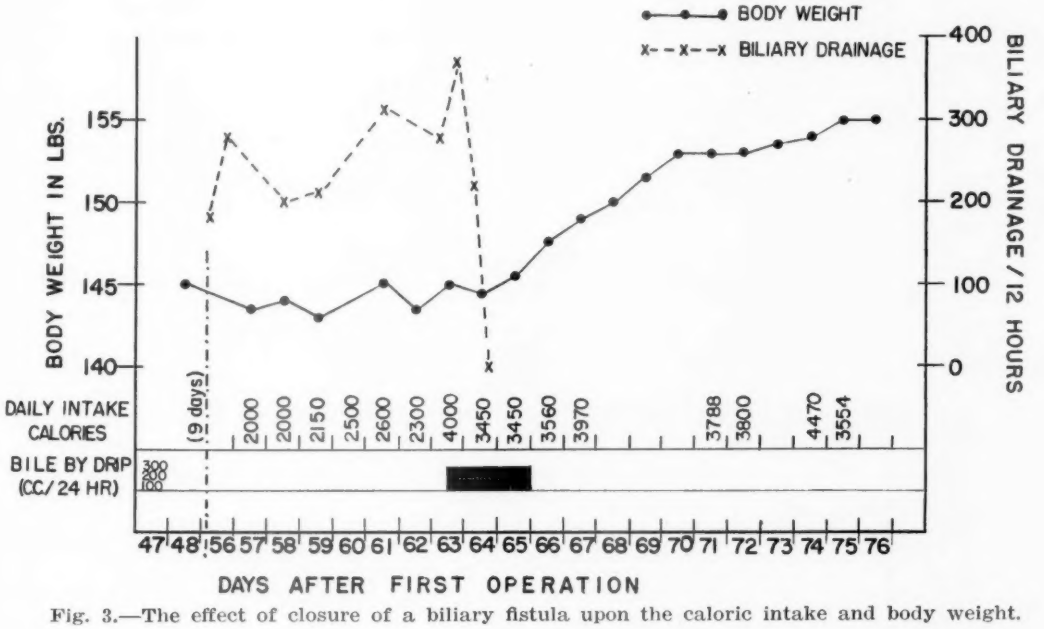

Fig. 3.—The effect of closure of a biliary fistula upon the caloric intake and body weight.

His data also illustrate well the adverse effect of a biliary fistula on the general nutritional status. Through the operation he had lost much weight, and despite every encouragement to eat he failed to gain. On the fifty-eighth day he was fed back bile with his meals. Curiously, it was after only a few days of this regime that his fistula closed completely. From then on there was a rapid gain in body weight, averaging one pound daily. Of course, in such patients, when bile is dripped in through a duodenal tube during and after meals, there are great improvement in appetite, digestion, and absorption, and a general feeling of well-being. Such reintroduction of bile into the alimentary tract is undoubtedly an important preparatory measure when operation for cure of a fistula is contemplated.

Clinical experience shows that contracting scar tissue or debris will eventually block the fistulous track. The head of pressure in the bile then

rises and it escapes through its natural outlet into the duodenum. But if this outlet is obstructed, for example, by an overlooked calculus, recurrent chills, fever, and jaundice result, since fistula bile is invariably infected.

Increased Flow From Dilated Duct System.—In Fig. 4 the twenty-seven operations have been divided into two groups, those at which the common bile ducts were grossly dilated and others. The average volumes drained are clearly greater from the dilated ducts. The explanation for this increased flow, where the duct system is dilated, is obscure. Bile pent up in the ducts must escape in the first few hours after the insertion of the drain and would not account for the persistently greater flow, which in some patients only reaches its maximum forty-eight to seventy-two hours postoperatively.

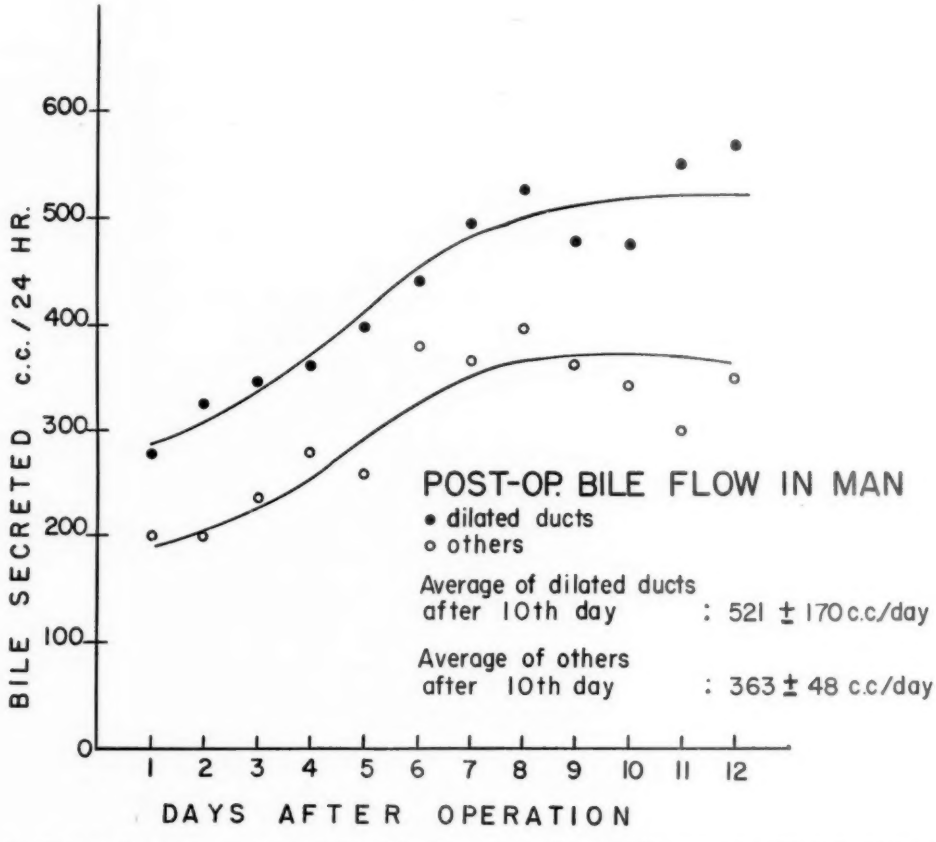

Fig. 4.—Comparison of average daily bile flow in patients with grossly dilated ducts and others.

It is possible that in certain types of biliary obstruction, free external drainage results in a release type of postoperative curve, the daily volume rising to high levels (of the order of 800 to 900 c.c.) before settling to the more usual level. This type of curve has been seen in four patients, suggesting that relief of obstruction may overshadow the depressing effect of operation on the secretory function of the liver. It is noteworthy that in several

of McMaster, Broun, and Rous's dogs, the fistula was temporarily obstructed and, upon relief of the obstruction, there was a considerable transient increase in bile flow.

There is another possible factor. Where the duct system is dilated, the area of the lining epithelial surface is greatly increased. Undoubtedly the lining membrane of the biliary passages can manufacture a small quantity of clear secretion. However, this does not appear to be a sufficient explanation for the increased volume flow in patients with dilated ducts.

The volume differences shown in Fig. 4 are of clinical importance even if we cannot explain them adequately, because the volume of bile drained in the patient with a fistula or T tube governs the weight of electrolyte lost from the body. As the volume drained daily may vary from 25 to 1,000 c.c., it is essential that the loss be measured, if restoration of fluid and electrolyte is to approximate the patient's requirement. A simple method of collecting the bile escaping from a fistula, and the serious consequences of failure to compensate for the resulting electrolyte loss, have been fully described elsewhere (Cass, Rundle, and Robson, 1955[4]).

DISCUSSION

It has been established that immediately after choledochostomy in man the secretion of bile is reduced by approximately one-half. During the following ten to twelve days, there is gradual recovery to a steady "normal" level of secretion. This is similar to the findings of McMaster and associates (1923) in dogs that during the first few days after establishing a biliary fistula, bile flow was scanty. Between three and seven days, it increased to an approximately normal level.

Like McMaster and co-workers we have found that this recovery of bile flow occurs independently of food intake. Thus the curve of increase was found to assume its usual shape in several patients who were maintained for prolonged periods on intravenous therapy.

Because their dogs were generally so fit forty-eight hours postoperatively, McMaster and associates ascribed the scanty postoperative flow to local factors, especially trauma of the ducts, rather than to general influences. However, it seems to us more likely that the reduced postoperative output results from a true functional depression of the liver. We have, in fact, evidence suggestive of depressed bile flow after one other major upper abdominal operation. Thus, in patients undergoing gastric resection, analysis of material aspirated from the gastric remnant postoperatively shows bilirubin to be absent, or present in only very low concentration, for thirty-six to seventy-two hours. Thereafter the concentration rapidly rises to 20 mg. per cent or more. Prolonged exposure of the liver to air at room temperature, intra-abdominal manipulations, including handling and retraction of the liver, and the impact of anesthetic agents might be factors in such depression of function.

SUMMARY

1. The secretion of bile immediately after choledochostomy in man is considerably depressed and recovery occurs only gradually during the first one to two weeks after operation.

2. Drainage of bile through a T tube in the common duct is virtually complete provided its vertical limb remains unobstructed.

3. Dilatation of the duct system at operation is associated with an increase in daily flow of bile drained.

4. The hepatic secretion of bile is continuous and not subject to diurnal variations.

5. Virtually total loss of bile through a biliary fistula may persist for long periods in the absence of obstruction at the lower end of the common duct.

REFERENCES

1. McMaster, P. D., Broun, G. O., and Rous, P.: Studies on Total Bile. I. Effects of Operation, Exercise, Hot Weather, Relief of Obstruction, Intercurrent Disease and Other Normal and Pathological Influences, J. Exper. Med. **37**: 395, 1923.
2. Hawkins, W. B., and Whipple, G. H.: Bile Fistulas and Related Abnormalities. Bleeding, Osteoporosis, Cholelithiasis and Duodenal Ulcers, J. Exper. Med. **62**: 599, 1935.
3. With, T. K.: Bilirubin and Urobilinoid Contents of Human Bile, Acta med. scandinav. **22**: 513, 1945.
4. Cass, M. H., Rundle, F. F., and Robson, B. M.: Electrolyte Losses With Biliary Fistula. The Post-choledochostomy Acidotic Syndrome, M. J. Australia **1**: 165, 1955.

STUDIES ON PANCREATITIS

II. Acute Pancreatic Necrosis Produced Experimentally by the Arthus Sensitization Reaction

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AUTOPSY studies show that extensive capillary and venous thromboses[1-3] are the most consistently demonstrable vascular lesions, in human acute pancreatic necrosis. However, the pathogenesis of these lesions still remains obscure although recent experimental work indicates that suppression of pancreatic blood flow may be an important primary factor in precipitating the necrotizing form of the disease.[4-7] The studies described herein demonstrate an experimental method of producing both acute interstitial pancreatitis and acute hemorrhagic pancreatic necrosis by means of the Arthus sensitization reaction. It will be shown that the type of pancreatitis produced is dependent on the degree of sensitization of the animal, and that the occurrence of the necrotic form of the experimental disease is associated with the development of extensive small vessel thrombosis.

MATERIALS AND METHODS

Animals.—Rabbits were used throughout these experiments because of the ease with which the Arthus reaction can be elicited in this species. The rabbits were market-bought 2- to 3-kilogram animals of both sexes and mixed breeds. The dogs were 5- to 8-kilogram mongrels of both sexes.

Ovalbumin.—The preparation used was albumin, egg (powder), supplied by General Chemical Company, New York.

Sensitization Procedure.—Rabbits were given an initial dose of 1 Gm. of albumin suspended in 20 c.c. saline solution intravenously. Thereafter, 200 mg. was given subcutaneously at five-day intervals. Intradermal skin testing with 10 mg. of albumin after about five or six weeks produced a gangrenous reaction in the majority of animals.

PREPARATION OF THE ANTIGEN FOR INTRADUCTAL INJECTION

Injection.—A 1 per cent solution of egg albumin was made in 0.9 per cent saline solution and its pH adjusted to 7.5 to 8.0 with 0.85 per cent NaOH. The solution was then centrifuged at high speed for thirty minutes and the supernatant removed and stored under sterile conditions using 1:1,000 Merthiolate as preservative. This stock solution, which on actual testing showed 0.6 Gm. protein per 100 c.c., was used for all intraductal injections.

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Intraductal Injection.—A constant pressure injection apparatus consisting of a 3-liter pressure bottle connected to a manometer and a small graduated fluid reservoir was used to deliver a known amount of fluid at constant pressure. The details of ductal cannulization in the rabbit were described in a previous paper.[5]

Sections.—Sections were fixed in formalin and stained by the hematoxylin and eosin method.

Fig. 1.—Rabbit No. 14. Showing extensive necrosis of pancreatic tissue and scattered foci of fat necrosis.

EXPERIMENTAL

1. *The Production of Acute Interstitial Pancreatitis in Moderately Sensitized Animals.*—Twelve animals were sensitized by the standard method described previously. By the fourth week the injection of 10 mg. of ovalbumin intradermally generally produced an acute inflammatory reaction marked grossly by redness and swelling without necrosis. One week after the dermal inflammatory reaction had subsided, a laparotomy was performed under Nembutal anesthesia and 0.5 c.c. of the standard albumin antigen was injected into the pancreatic duct of eight of the rabbits at a pressure of 20 mm. Hg. The remaining four rabbits were used as controls and received heat-denatured ovalbumin. The duct was then ligated and the abdominal incision closed. The rabbits recovered rapidly from anesthesia and appeared active and in good health

until sacrificed forty-eight hours after intraductal injection. At autopsy, the pancreas appeared moderately edematous; there was no hemorrhage, fat necrosis, or accumulation of ascitic fluid. Microscopically, there was diffuse interstitial edema and extensive polymorph infiltration without necrosis of acinar cells. In some areas there was marked swelling and increased eosinophilia of collagen fibers.

Hemorrhage was uniformly absent, although punctate areas of fat necrosis were occasionally seen. The four control animals showed ductal dilation and mild interstitial infiltration by polymorph leukocytes, which in no case approached the severity of the interstitial reaction in the animals receiving unheated albumin.

2. *The Production of Acute Hemorrhagic Pancreatic Necrosis in Highly Sensitized Animals.*—Sensitization in this group of twelve rabbits was carried on for five to eight weeks until the intradermal injection of 0.5 c.c. of the standard ovalbumin solution resulted in the classical gangrenous necrosis of the fully developed Arthus reaction. One week later an injection of 0.5 c.c. ovalbumin solution was made into the pancreatic duct of eight animals at a pressure of 20 mm. Hg. Four control animals received heat-denatured ovalbumin. The results are summarized in Table I, whence it will be seen that one rabbit died at eighteen hours, one at thirty hours, and one at thirty-six hours. The remainder were sacrificed at forty-eight hours. At autopsy, seven of these eight animals showed extensive miliary areas of fat necrosis and large 2 to 8 mm. areas where the normal finely reticular structure of the pancreas was transformed into a structureless swollen coagulum (Fig. 1). Hemorrhage was grossly evident in only four animals.

Microscopically, there were segmental areas of massive pancreatic necrosis (Fig. 2). These areas were composed of a large central zone where the lobules of acinar tissue, ducts, and blood vessels showed only the eosinophilic ghosts of their former structure. It is noteworthy that in these areas of maximal destruction the small veins appeared to be completely occluded by laminated thrombus. At the periphery of the necrotic areas the pancreatic acini were separated by an extensive infiltration of polymorph leukocytes, many of which were advanced stages of necrobiosis. In this peripheral zone, capillaries and venules, completely occluded by hyalin thrombus, were commonly seen (Fig. 3). The walls of these vessels occasionally showed areas of necrosis and infiltration by leukocytes. Throughout the sections there was prominent eosinophilic swelling of collagenous tissue and perivascular deposition of fibrinoid material.

These thrombotic vascular lesions were similar to those previously described by Opie[8] in the fully developed gangrenous dermal Arthus reaction. Pancreatic necrosis regularly occurred in zones where the majority of small vessels showed thrombotic occlusion and, conversely, in the relatively less involved parts of the pancreas thrombotic lesions were uniformly absent, and leukocytic infiltration was quite prominent.

TABLE I. THE PRODUCTION OF ACUTE PANCREATIC NECROSIS IN RABBITS HIGHLY SENSITIZED TO OVALBUMIN*

RABBIT NO.	SUBSTANCE INJECTED	DURATION OF LIFE AFTER INTRADUCTAL INJECTION	AUTOPSY FINDINGS	
			GROSS	MICROSCOPIC
13	Ovalbumin 0.5 c.c.	18 hr.	Minimal fat necrosis; marked edema and small areas of pancreatic necrosis	Focal coagulation necrosis with surrounding polymorph reaction; marked edema
14	Ovalbumin 0.5 c.c.	36 hr.	Extensive fat necrosis, 2-8 mm. areas of pancreatic necrosis; slight hemorrhage	Extensive coagulation necrosis of large areas; prominent thrombotic lesion and polymorph reaction
15	Ovalbumin 0.5 c.c.	Sacrificed at 48 hr.	Extensive fat necrosis, large areas of pancreatic necrosis; no hemorrhage	Similar to No. 14
16	Ovalbumin 0.5 c.c.	Sacrificed at 48 hr.	Pancreatic edema; no necrosis; no hemorrhage	Marked interstitial polymorph reaction; no parenchymal necrosis
17	Ovalbumin 0.5 c.c.	Sacrificed at 30 hr.	Focal fat necrosis, multiple 2-4 mm. areas of pancreatic necrosis and surrounding hemorrhage	Focal areas of coagulation necrosis with surrounding polymorph reaction
18	Ovalbumin 0.5 c.c.	Sacrificed at 48 hr.	Extensive fat necrosis, large areas of pancreatic necrosis; no hemorrhage	Similar to No. 14
19	Ovalbumin 0.5 c.c.	Sacrificed at 48 hr.	Focal fat necrosis, multiple 2-4 mm. areas of pancreatic necrosis; moderate surrounding hemorrhage	Small areas of coagulation necrosis with surrounding hemorrhage
20	Ovalbumin 0.5 c.c.	Sacrificed at 48 hr.	Scanty fat necrosis single 0.5 mm. area of pancreatic necrosis and hemorrhage	Large area of complete coagulation necrosis with prominent thrombotic occlusion of related veins and capillaries
21	Heat-denatured ovalbumin 0.5 c.c.	Sacrificed at 48 hr.	Pancreatic edema; no necrosis, no hemorrhage	Mild interstitial pancreatitis; moderate ductular dilatation
22	Heat-denatured ovalbumin 0.5 c.c.	Sacrificed at 48 hr.	Pancreatic edema; no necrosis, no hemorrhage	Mild interstitial pancreatitis; moderate ductular dilatation
23	Heat-denatured ovalbumin 0.5 c.c.	Sacrificed at 48 hr.	Pancreatic edema; no necrosis, no hemorrhage	Mild interstitial pancreatitis; moderate ductular dilatation
24	Heat-denatured ovalbumin 0.5 c.c.	Sacrificed at 48 hr.	Pancreatic edema; no necrosis, no hemorrhage	Mild interstitial pancreatitis; moderate ductular dilatation

*All injections into the pancreatic duct were made at pressures ranging between 20 and 25 mm. Hg. At the conclusion of the injection the pancreatic duct was ligated.

In the control animals receiving heat-denatured albumin there were no deaths, and when the animals were sacrificed at forty-eight hours the pancreas appeared slightly edematous. Microscopically, there was slight interstitial edema, ductular dilatation, and slight polymorph infiltration without necrosis of parenchymal cells or vascular thromboses.

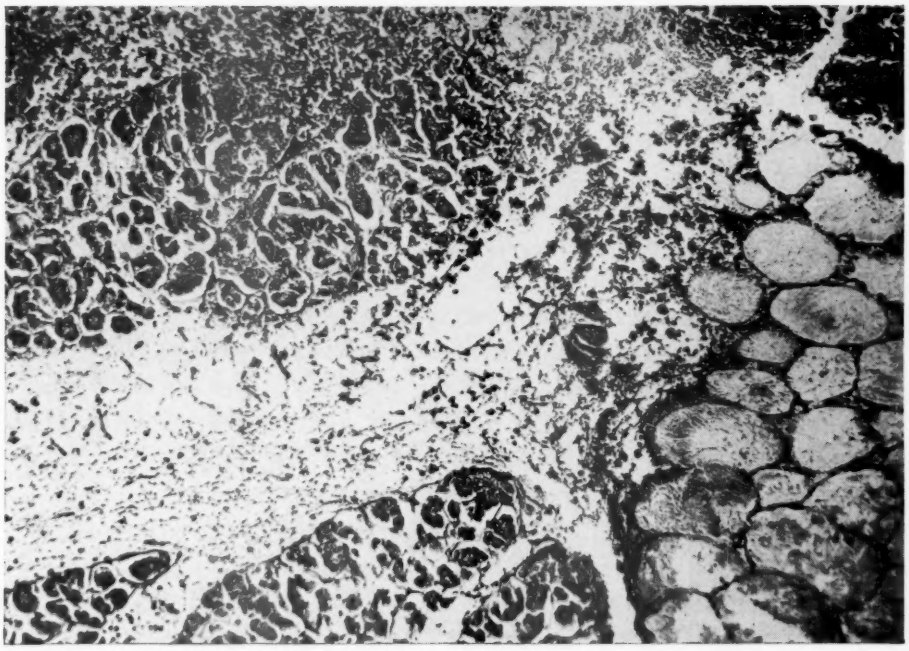

Fig. 2.—Rabbit No. 14. Low-power view of parenchymal and fat necrosis with peripheral polymorph reaction.

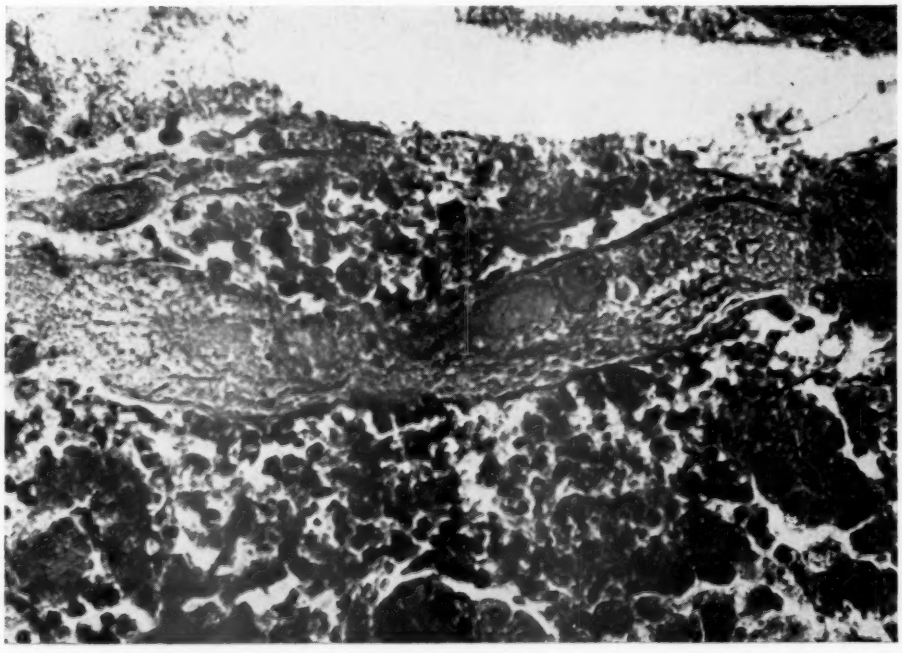

Fig. 3.—Hyaline thrombosis and polymorph reaction in small vessel at the margin of an area of coagulation necrosis.

DISCUSSION

The studies described herein demonstrate that pancreatitis may be regularly produced in animals suitably sensitized to a foreign protein. The lesion is, in effect, a local manifestation of the Arthus reaction and has certain features which may be important in the understanding of the naturally occurring disease.

Particular attention was paid to careful control of injection pressure during these experiments and in no instance did the pressure exceed 25 mm. of mercury. The quantity of antigen needed to produce a great response in a highly sensitized animal is minute, and it is conceivable that such small amounts of albumin might gain access to the interstitial tissue by direct diffusion across the basement membrane between adjacent ductular or acinar cells. These pancreatic Arthus phenomena offer interesting parallels in the field of human pancreatitis, where the two common forms of the disease, the interstitial and the necrotic, differ among other things in the uniform absence of thrombotic lesions in the former type and their frequent presence in the latter. That these thrombotic lesions are, in all probability, the factor responsible for conversion of the inflammatory reaction to the necrotic one is suggested by the ameliorating effect of heparin on the dermal necrosis of the fully developed Arthus reaction, as shown by Gregoire.[9] Moreover, in the present experiments the areas of parenchymal necrosis were consistently related to thrombosed vessels, whereas these vascular lesions were conspicuously absent from areas showing a predominantly interstitial reaction in the same pancreas. The morphologic picture of this form of pancreatic necrosis resembles that of the human disease in many respects. There are large areas of complete coagulation necrosis of pancreatic parenchyma and blood vessels, and focal areas of fat necrosis. The indiscriminate and random necrosis of the pancreas and the sharp line of demarcation between necrotic and viable tissue are quite characteristic of both the experimental and the human disease. The Arthus lesion differs from the majority of human cases in the intensity of the cellular reaction at the periphery of the lesion and the frequent deposition of fibrinoid material in this area. It is also of interest that the capillary and venular thromboses found at the periphery of the experimental lesion are quite similar to those first observed by Opie[3] at the boundary of viable and necrotic pancreatic tissue in human autopsy cases.

Whether allergy plays any part in the pathogenesis of the human disease is quite unknown at the present time, although clinical observations suggesting food allergy as a causative mechanism are reported by Shaffer.[12] The data reported, however, are not conclusive. Hypothetically, the possibility also exists of sensitization to bacteria or bacterial products. However, the only well-documented case where an antigen-antibody reaction may be directly implicated is Ackerman's[11] report of acute hemorrhagic pancreatic necrosis occurring in a patient after a mismatched blood transfusion. It should be pointed out that in Ackerman's case, as well as in the experimental work described here, the only inference which may be drawn at the present time is that small vessel thrombosis may be a precipitating mechanism in some cases of pancreatic necrosis.

SUMMARY

In order to study the role of primary small vessel thrombosis in the causation of acute hemorrhagic pancreatic necrosis the Arthus reaction was induced in the pancreas of rabbits in various stages of sensitization.

In the moderately sensitized rabbit acute nonfatal interstitial pancreatitis was produced.

Ductal injection of antigen in the highly sensitized rabbit produced a severe pancreatic necrosis, which was fatal in three animals. The capillaries and venules in and about the areas of pancreatic necrosis were commonly occluded by hyaline, or leukocyte fibrin thrombi. This lesion was uniformly absent in animals showing extensive interstitial pancreatitis.

The two types of experimental pancreatitis described bear a striking resemblance to the interstitial and necrotic forms occurring in human beings. The role of allergy in the causation of this disease is as yet unexplored.

REFERENCES

1. Smyth, C. J.: Etiology of Acute Hemorrhagic Pancreatitis With Special Reference to the Vascular Factors, Arch. Path. **30**: 651-669, 1940.
2. Thal, A. P., and Molestina, J. E.: Clinical and Pathological Study of 51 Cases of Pancreatitis. To be published.
3. Opie, E. L.: Disease of the Pancreas: Its Cause and Nature, ed. 1, Philadelphia, 1903, J. B. Lippincott Company, p. 128.
4. Popper, H. L., Necheles, H., and Russel, K. C.: Transition of Pancreatic Edema Into Pancreatic Necrosis, Surg., Gynec. & Obst. **87**: 79, 1948.
5. Thal, A. P., and Brackney, E.: Acute Hemorrhagic Pancreatic Necrosis Produced by Local Shwartzman Reaction, J. A. M. A. **155**: 569-574, 1954.
6. Thal, A. P., and Molestina, J. E.: Pancreatitis. III. Fulminating Hemorrhagic Pancreatic Necrosis Produced by Means of Staphylococcal Toxin, Arch. Path., 1955. In press.
7. Thal, A. P.: Pancreatitis. IV. The Pathogenesis of Bile Pancreatitis, Fundamental Forum on Surgical Problems, Philadelphia, 1954, W. B. Saunders Company. In press.
8. Opie, E. L.: Pathogenesis of the Specific Inflammatory Reaction of Immunised Animals. (Arthus Phenomenon), J. Immunol. **9**: 259-268, 1924.
9. Gregoire, C.: Influence de l'héparine sur les réactions d'anaphylaxie locale cutanée (phénomène d' Arthus), Arch. internat. pharmacodyn. et thérap. **72**: 76-92, 1946.
10. Mann, F. C., and Giordano, A. S.: The Bile Factor in Pancreatitis, Arch. Surg. **6**: 1, 1923.
11. Ackerman, L. V.: Acute Pancreatitis Following Blood Transfusion, Arch. Path. **34**: 1065, 1942.
12. Shaffer, J.: Allergic Pancreatitis, Permanente Found. M. Bull. **6**: 204, 1948.

THE CHOLEDOCHO- AND PANCREATICODUODENAL JUNCTIONS IN THE CHIMPANZEE

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BECAUSE of the importance of the sphincter of Oddi, physiologically and clinically, any new information about its structure or function in primates should be of interest. Some years ago, through the courtesy of Dr. Arthur Kirschbaum and other members of the Yale Department of Anatomy, I obtained upper portions of the gut tract of two chimpanzee fetuses which had been preserved in formalin and which were in such good condition that they could be sectioned serially and stained with the smooth muscle dye, azocarmine. The first was a 126-day fetus that had been aborted. It had a crown-rump length of 130 millimeters and weighed 210 grams. (According to Tinklepaugh, 1933, the gestation period of the chimpanzee is approximately 246 days, or 8 months, and the fetus at term weighs approximately 2,260 grams.) The mother was small for a chimpanzee and had had three interrupted pregnancies. The second fetus had an age of 167 days and a CR length of 230 millimeters. These two specimens will be referred to hereafter as "Chimp A" and "Chimp B," respectively.

The gross appearance of the major and minor papillae of "Chimp B" are shown in Fig. 1. Selected transverse sections through the corresponding portion of the duodenum of "Chimp A" are shown in Figs. 2 to 10. The latter should be compared with the two sets of plates of human fetuses made by Schwegler and Boyden in 1937. The first of these sets (Figs. 12 to 17, 1937b) was taken from a 16-week fetus (105 mm. CR length) and therefore slightly younger than "Chimp A." The second set (Figs. 10 to 21, 1937c) was from an 8-month, 430 mm. (CH) fetus, and therefore considerably older than "Chimp B."

THE CHOLEDOCHODUODENAL JUNCTION

It will be recalled that in human fetuses approaching term the intrinsic musculature in the junctional region forms a continuous sheath of smooth muscle around the bile duct from just outside the choledochal window of the duodenum to the point in the submucosa where bile and pancreatic ducts unite to form the ampulla of Vater. This is the *sphincter choledochus.* In human embryos it appears about the ninth or tenth week of menstrual age (41 to 45 mm. embryos) as a differentiation of mesenchyme around that portion of the bile duct that is entering the choledochal window in the tunica muscularis of the gut. It thus appears some four weeks later than the muscular tunic of

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the duodenum. From this level it differentiates from the mesenchyme, progressively, in both directions: namely, up along the bile duct for a short distance, and down the duct, along its intramural course, as far as the ampulla.

The time relations are of importance, for some observers have mistaken earlier concentrations of mesenchyme for the sphincter itself and have thereby drawn erroneous conclusions about it. For example, in a 27 mm. human embryo Kirk (1944) described "circularly disposed fibres . . . in the intraduodenal portion of the duct wall . . . that are continuous with the circular muscle differentiating in the wall of the intestine (Pl. 3, Fig. 7)." In a later article, based on the same specimen (1948, Figs. 3 to 5), he stated that the extramural portion of the sphincter is derived from the longitudinal muscle of the gut, and the intramural portion from the circular muscle of the gut.

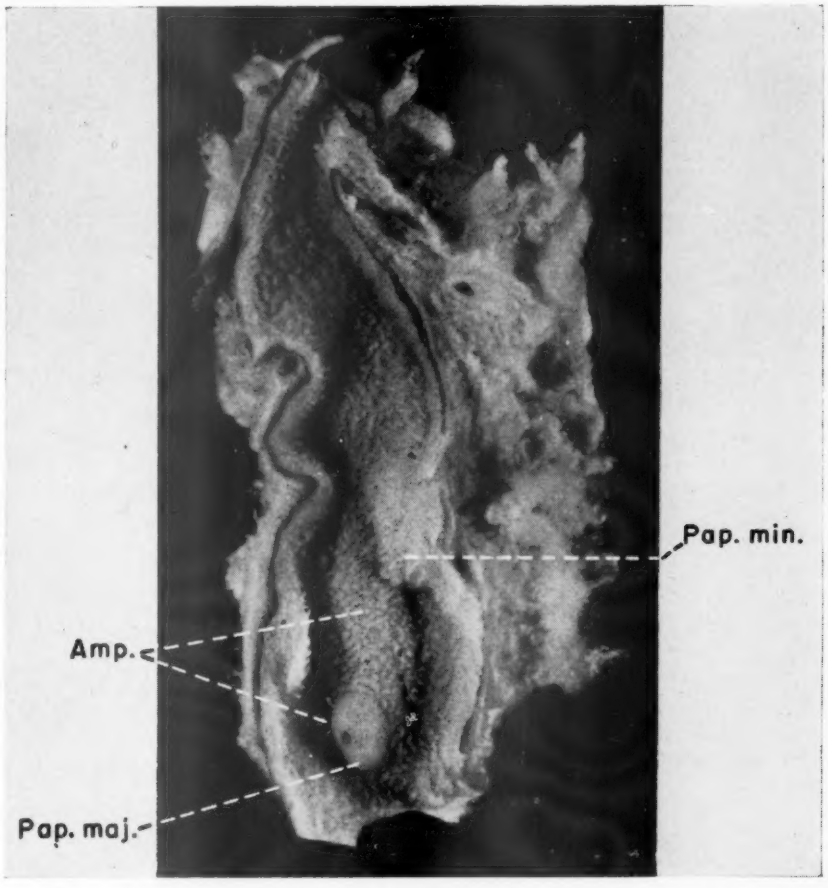
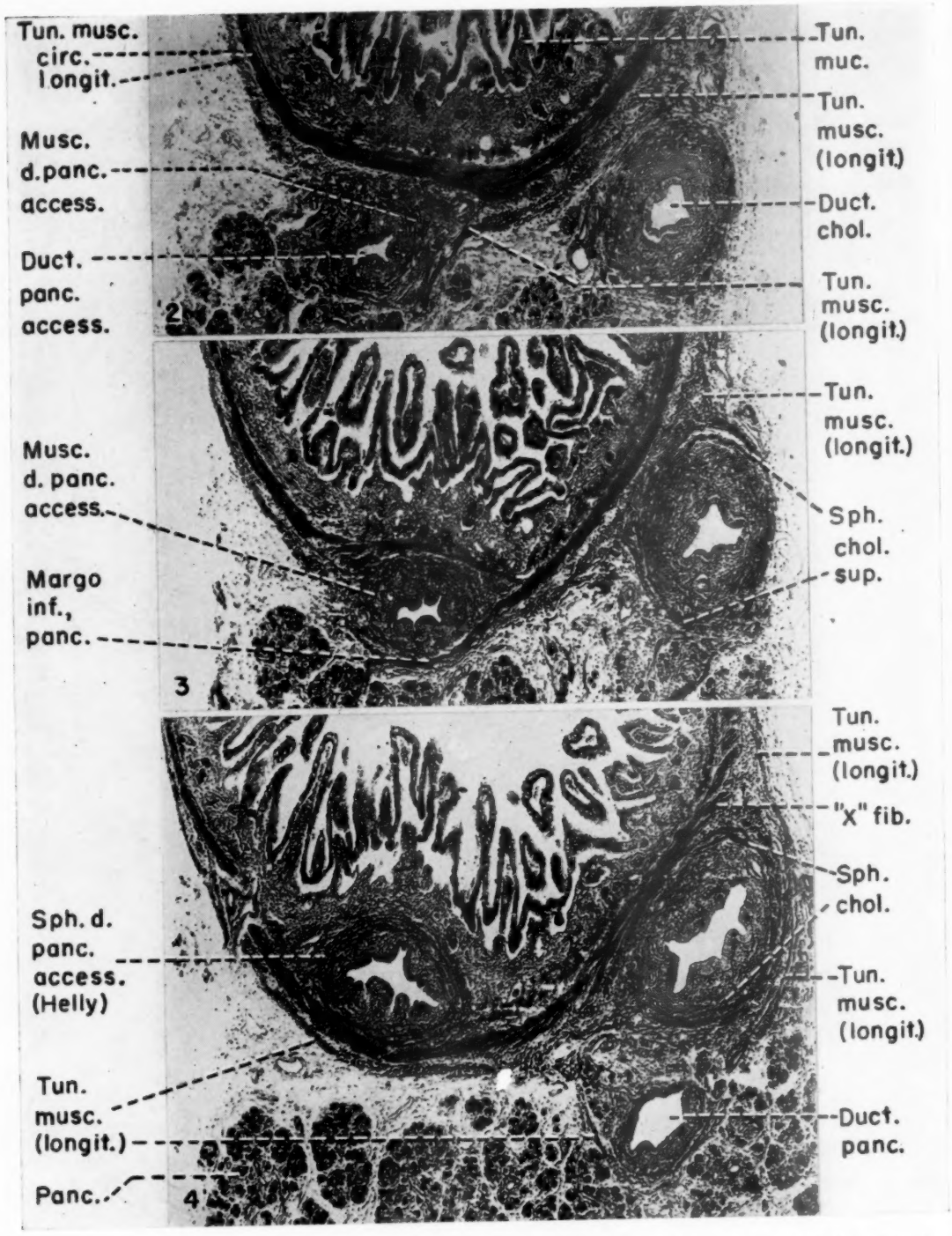


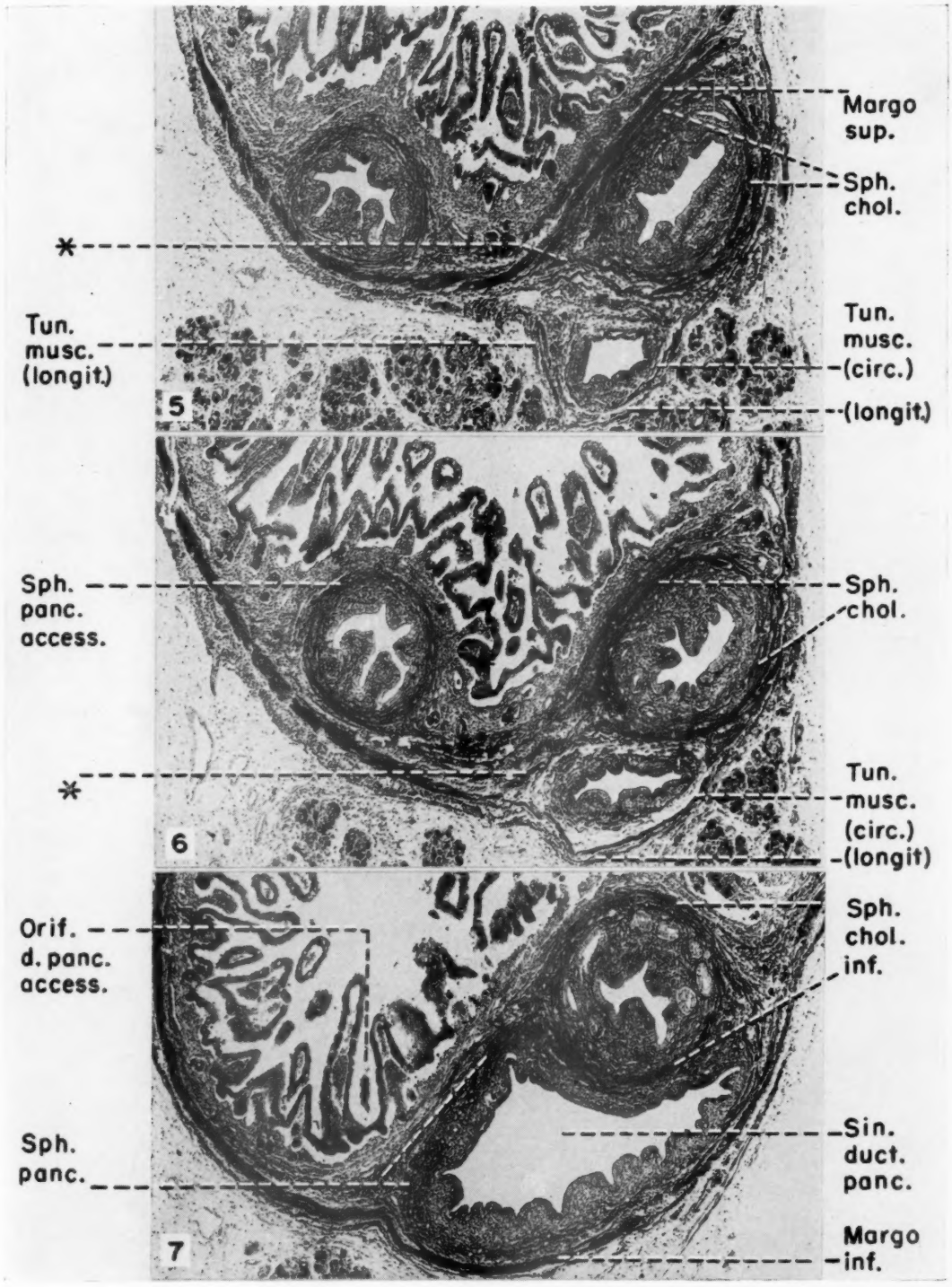
Fig. 1.—The opened duodenum of "Chimp B" (167-day fetus) showing relative size and position of the major and minor papillae. Note area that is bare of villi at end of major papilla, the great length of the ampulla of Vater, and the large size of the minor papilla. (×6; reduced ⅓.)

However, this, which he assumed to be the sphincter itself, is merely a condensation of mesenchyme around both bile and pancreatic ducts which is contiguous peripherally with the intestinal muscle. Helly (1900) had seen a similar arrangement in a 28.5 mm. human embryo and labeled it "musculus

sphincter''—an error of interpretation to which F. T. Lewis called attention in 1911-1912. The sphincter muscle, however, does not begin to form until some two weeks later (in 41 to 45 mm. fetuses). It is only at this time, and

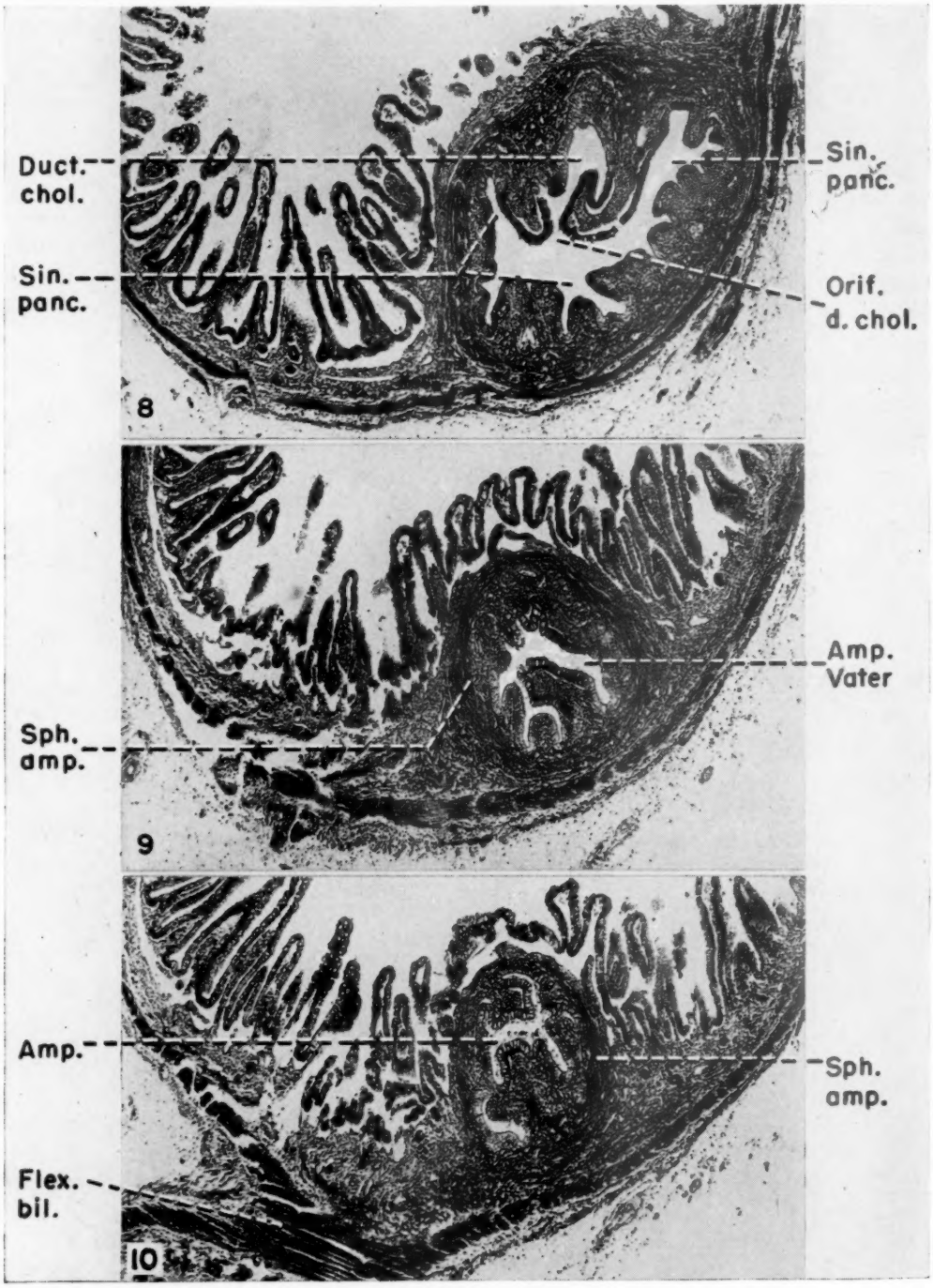


Figs. 2-10.—Transverse sections through the duodenum of "Chimp A" (126-day fetus) showing the passage of bile and pancreatic ducts through the intestinal wall. For details, see text.



Figs. 5-7. *(For legend see opposite page.)*

from then on, that the true relation of the sphincter to the intestinal muscle can be studied. Unfortunately, these errors of interpretation have been used to discredit the fact that the sphincter choledochus is essentially an independent



Figs. 8-10. (*For legend see page 920.*)

structure. Thus in the latest edition of Cunningham (p. 667) we read, "Opinion is still divided as to how far, *if at all* [my italics] these encircling fibres can be regarded as intrinsic sphincters, structurally and functionally independent of the intestinal muscles."

A second cause of confusion may be attributed to the fact that when the sphincter first differentiates from mesenchyme in the choledochal window the ducts seem to induce a sprouting of muscle fibers from the adjacent intestinal wall which connects the margins of the window with the intrinsic muscular sheath around the ducts (cf. Schwegler and Boyden, 1937b, Fig. 4). These join the longitudinal fibers that anchor the bile and pancreatic ducts to the window and assist in erecting the major papilla (Kreilkamp and Boyden, 1940). Also, they are the fibers that are responsible for giving an impression of continuity of the two musculatures. However, they can be distinguished from the main sheath since this develops from window to ampulla by progressive differentiation of mesenchyme into circular muscle fibers (Schwegler and Boyden, 1937b, Fig. 5). Bergh and Layne have studied this sphincter experimentally in cholecystectomized and intubated patients. By ingenious methods of recording simultaneously the action of sphincter and duodenal musculature, they have demonstrated that the sphincter choledochus can act independently of the duodenal muscle, and that spasms of the sphincter may even produce biliary colic.

The sections through the duodenum of the available chimpanzee fetuses will not, of course, show the initial stages in the formation of the sphincter, but they do bring out points of agreement as well as interesting differences between the human and the subhuman primate.

Beginning with Fig. 2, the common bile duct (*Duct. chol.*) may be seen descending toward the intestinal wall. The viewer is looking at the pars descendens of the duodenum with the accessory duct to his left and the bile duct to his right. (For orientation, compare with Fig. 9 of Schwegler and Boyden, 1937a, and Fig. 9, 1937b). One major difference will be noted. In the human fetus the longitudinal muscle of the duodenum withdraws from the region between the gut and the bile duct, leaving a large diamond-shaped hiatus (cf. Fig. 9, Schwegler and Boyden, 1937b). In the chimpanzee it remains and participates in the formation of the sphincter (*Tun. musc.* [*longit.*], Fig. 2).

A little lower down (Fig. 3) the first circular fibers are appearing around the bile duct. These are forming the extramural portion of the sphincter choledochus superior. The longitudinal muscle of the gut may be seen creeping up along the sides of the sphincter. In the older "Chimp B" it will surround the sphincter (at level of Fig. 3), and then withdraw in front of it as the pancreatic duct converges upon the bile duct.

In Fig. 4, the sheath is in contact with the margo superior of the choledochal window (cf. Fig. 9, Schwegler and Boyden, 1937b). Here the circular muscle of the gut is being stimulated to give off "X" fibers (cf. 1937b, Fig. 4). These will develop into the "connecting" and "reinforcing" fibers described by Kreilkamp and Boyden (their Figs. 1 to 3). But at this level we note an-

other difference between the human and chimpanzee fetuses. In the latter the longitudinal muscle of the gut covers both bile and pancreatic ducts as soon as they approach each other. The longitudinal layer is soon accompanied by strands from the circular layer (Figs. 5 and 6). This high envelopment of the ducts suggests the condition found in subprimate mammals (guinea pig, dog, and cat), where both longitudinal and circular muscles of the gut form funnels that enclose the ducts (cf. Fig. 1, Boyden, 1937). In contrast, the human ducts have to pierce only the circular muscle layer of the duodenum, and this is accomplished through a narrow transverse slit whose superior and inferior (or inner and outer) margins are virtually in the same transverse plane (Schwegler and Boyden, 1937b, Fig. 10).

In Figs. 5 and 6 the circular muscle of the gut now appears outside the pancreatic duct (*Tun. musc.* [*circ.*]). This corresponds to the margo inferior of the choledochal window of the human fetus (cf. Fig. 9, Schwegler and Boyden, 1937b). However, the muscle bundle marked by an asterisk—a strand of circular fibers lying *between* bile and pancreatic ducts—is not present in man (cf. Figs. 13 and 15, Schwegler and Boyden, 1937c).

In Fig. 7 the two ducts have passed through the windows in the tunica muscularis of the gut and are traversing the submucosa. The sphincter choledochus now appears as a thick, well-developed band that completely encircles the bile duct. In addition there are fibers that could function as a sphincter pancreaticus. These swing from the muscle layer between the two ducts to the sides of the pancreatic duct, where they join the longitudinal fascicles. In the 8-month human fetus no such fibers could be recognized (cf. Fig. 16, Schwegler and Boyden, 1937c), and in the adult they were seen in only four of twelve macerated specimens (Kreilkamp and Boyden).

Perhaps the most striking feature in the chimpanzee fetuses (Fig. 7) is the expansion of the intramural portion of the pancreatic duct—a segment which I have termed the *sinus pancreaticus.* At the level where the two ducts become confluent (Fig. 8) the sinus is nearly three times as wide as the bile duct, so that the latter appears to be tributary to the former. One wonders if this narrowing of the bile duct as it approaches the confluence could have any physiologic significance. Certainly the sphincter choledochus could close the orifice very effectively. It will be recalled that in man this is not only the sphincter which causes the filling of the gall bladder but also the one that may hypertrophy in the presence of stones, leading to their impaction in the intramural portion of the bile duct (Boyden, 1941).

As in the human fetus, the two ducts become surrounded by a common sheath of fibers just before they become confluent (Fig. 8). This is the beginning of the *sphincter ampullae.* In man this is poorly developed in fetal stages (cf. Figs. 17 and 18, Schwegler and Boyden, 1937c) and becomes of consequence only in that fifth or sixth of adult specimens in which the ampulla persists as a sizable segment (Kreilkamp and Boyden). In such instances contraction of this muscle may create a common pathway between bile and pancreatic ducts which becomes manifest roentgenologically when the T tube of intubated patients is injected with radiopaque fluid.

Fig. 9 shows the main portion of the sphincter ampullae. Here it is as well developed as the ring musculature around the terminal portion of the bile duct (compare Figs. 7 and 9).

Another striking difference between the chimpanzee and human fetus is the differing angle which the ampulla makes with the tunica muscularis. In man, the ampulla moves away from the circular muscle of the gut (cf. Figs. 9 to 17, Schwegler and Boyden, 1937b, and Figs. 17 to 20, 1937c). Such a papilla can be erected. In the chimpanzee, the ampulla remains parallel and close to the circular muscle of the gut all the way to the papillary orifice (Figs. 8 to 10). Perhaps as a consequence of this the intestinal muscle continues to send circular strands into the right and left sides of the ampulla. These turn longitudinally, at once, suggesting that their function is to shorten the ampulla—a substitute, as it were, for erection of the papilla. Incidentally, the ampulla of "Chimp B" is very long (Fig. 1), constituting six-thirteenths of the intramural portion of the biliary passage. At the end, the papilla is bare of villi (Fig. 1). A similar bare area is visible in the human fetus (cf. Fig. 19, Schwegler and Boyden, 1937c).

THE PANCREATICODUODENAL JUNCTION

As in man, the ductus pancreaticus accessorius enters the duodenum above the level of the bile duct. In the adult the two sites of junction have grown some distance apart, but in the fetus it is possible to see both sets of ducts in the same section. Thus, in Fig. 2, accessory pancreatic and bile ducts are approaching the duodenum at nearly the same level. A sheath of intrinsic muscle fibers surrounds the duct (*Musc. panc.*). In "Chimp B," these are mostly longitudinal at this level.

In Fig. 3, the accessory duct is descending between the superior and inferior margins of the pancreatic window or fenestra.

In Fig. 4, the duct lies in the submucosa and is surrounded by the sphincter first described by Helly (1899). This sheath of muscle reaches its greatest development in the segment of the duct that lies in the submucosa. At this level (Fig. 6) it is completely separated from the circular muscle of the duodenum. Comparison of the human and chimpanzee sphincters of Helly will be made in a subsequent article dealing with human accessory duct.

DISCUSSION

Serial sections through the pars descendens duodeni of two chimpanzee fetuses (aborted at 4 and 5.5 months in a gestation period normally covering 8 months) reveal the presence of a well-developed sphincter choledochus and sphincter ampullae along the intramural course of the bile passages.

The purpose of this investigation has been to compare the development of these sphincters in man and a subhuman primate in the expectation that our understanding of the human structures might be broadened, even as an earlier study of mammalian biliary tracts had provided a means of classifying acces-

sory gall bladders in man (Boyden, 1926). Fetal specimens were preferred since the essential pattern is more easily comprehended in developmental stages.

Six striking differences were observed between the chimpanzee and human choledochoduodenal junctions: *first,* the widening of the submucosal segment of the pancreatic duct into a sinus pancreaticus and the narrowing of the bile duct at its confluence with the sinus; *second,* the participation of the longitudinal muscle layer of the duodenum in the formation of the sphincter choledochus superior; *third,* the high envelopment of both bile and pancreatic ducts by the longitudinal and circular muscles of the gut, thus creating a short muscular funnel through which both ducts must pass to reach the submucosa; *fourth,* the presence of strong bands of circular muscle running through the space between the bile and pancreatic ducts as they traverse the window; *fifth,* the precocious development and great length of the sphincter ampullae; *sixth,* the continuous contribution of the circular muscle of the gut to the longitudinal muscle of the ampulla.

From these observations it would appear that both man and the chimpanzee have well-developed intrinsic sphincters of the bile duct but that the choledochoduodenal junction of the chimpanzee is much more complicated than its human counterpart, and that it is somewhat intermediate in structure between that of man and the laboratory mammals, in that its upper portion does receive contributions from the intestinal musculature and does pass through a funnel in the muscular tunic of the duodenum. Previously, the rate of emptying of the gall bladder in the macaque had been found to be more like that of man than the cat (Boyden, 1932), but in structure the biliary tract of the monkey and cat resembled each other more closely. In view of these considerations one cannot help wondering whether the relative simplicity of the human choledochoduodenal junction may not reflect the virtual emancipation of the human biliary tract from motor control by the autonomic nervous system. It may be recalled that evacuation of the human gall bladder induced by a meal of egg yolk cannot be reflexly inhibited, as in the cat, by faradic stimulation of the gut (Boyden and Rigler, 1934) and that vagotomy in man as contrasted with that in cats does not diminish the normal rate of emptying of the gall bladder (Johnson and Boyden, 1952). If such be the case, has not the time come to discard the concept of biliary dyskinesia which was originally based on animal experimentation, unless it be shown that dysfunction in man is mediated by a hormonal mechanism? In any event, it is clear that in both man and the chimpanzee there exists a substantial submucosal sphincter choledochus that is far better developed in these forms than in the laboratory mammals and bears no resemblance to what John Homans referred to facetiously, in his textbook of surgery, as the "mythical sphincter of Oddi."

REFERENCES

Bergh, G. S., and Layne, J. A.: A Demonstration of the Independent Contraction of the Sphincter of the Common Bile Duct in Human Subjects, Am. J. Physiol. **128**: 690-694, 1940.

Boyden, E. A.: The Accessory Gallbladder. An Embryological and Comparative Study of Aberrant Biliary Vesicles Occurring in Man and the Domestic Mammals, Am. J. Anat. **38**: 177-232, 1926.

Boyden, E. A.: Emptying of the Gall Bladder in Monkeys, Proc. Soc. Exper. Biol. & Med. **29**: 1104-1105, 1932.

Boyden, E. A.: The Sphincter of Oddi in Man and Certain Representative Mammals, SURGERY **1**: 25-37, 1937.

Boyden, E. A.: Hypertrophy of the Sphincter Choledochus, SURGERY **10**: 567-571, 1941.

Boyden, E. A., and Rigler, L. G.: A Cholecystographic and Fluoroscopic Study of the Reaction of the Human Gall Bladder to Faradic Stimulation of the Stomach and Duodenum, Anat. Rec. **59**: 427-447, 1934.

Cunningham's Text-book of Anatomy, ed. 9, edited by J. C. Brash, London, New York, 1951, Oxford University Press.

Helly, K. K.: Die Schliessmuskulatur und den Mündungen des Gallen- und der Pankreasgänge, Arch. mikr. Anat. **54**: 614-621, 1899.

Helly, K. K.: Zur Entwickelungsgeschichte der Pankreasanlagen und Duodenalpapillen des Menschen, Arch. mikr. Anat. **56**: 291-308, 1900.

Homans, J.: A Text Book of Surgery (l.c., p. 879), ed. 6, Springfield, 1948, Charles C Thomas, Publisher.

Johnson, F. E., and Boyden, E. A.: The Effect of Double Vagotomy on the Motor Activity of the Human Gall Bladder, SURGERY **32**: 591-601, 1952.

Kirk, J.: Observations on the Histology of the Choledocho-duodenal Junction and the Papilla Duodeni, With Particular Reference to the Ampulla of Vater and the Sphincter of Oddi (l.c., Fig. 7), J. Anat. **78**: 118-120, 1944.

Kirk, J.: The Applied Anatomy of the Gall Bladder and Extra-hepatic Biliary Passages With Special Reference to Their Development (l.c., Figs. 3-5), Ann. Roy. Coll. Surgeons England **3**: 132-138, 1948.

Kreilkamp, B. L., and Boyden, E. A.: Variability in the Composition of the Sphincter of Oddi. A Possible Factor in the Pathologic Physiology of the Biliary Tract, Anat. Rec. **76**: 485-497, 1940.

Layne, J. A., and Bergh, G. S.: An Experimental Study of Pain in the Human Biliary Tract Induced by Spasm of the Sphincter of Oddi, Surg., Gynec. & Obst. **70**: 18-24, 1940.

Lewis, F. T.: The Development of the Liver. Development of the Pancreas, in vol. 2, pp. 403-445, of Keibel and Mall, Manual of Embryology, Philadelphia, 1912, J. B. Lippincott Company.

Schwegler, R. A., Jr., and Boyden, E. A.: The Development of the Pars Intestinalis of the Common Bile Duct in the Human Fetus, With Special Reference to the Origin of the Ampulla of Vater and the Sphincter of Oddi.
I. The Involution of the Ampulla, Anat. Rec. **67**: 441-468, 1937a.
II. The Early Development of the Musculus Proprius, Anat. Rec. **68**: 17-42, 1937b.
III. The Composition of the Musculus Proprius, Anat. Rec. **68**: 193-220, 1937c.

Tinklepaugh, O. L.: Sex Cycles and Other Cyclic Phenomena in a Chimpanzee During Adolescence, Maturity and Pregnancy, J. Morphol. **54**: 521-548, 1933.

EXPERIENCES WITH THORACOLUMBAR SYMPATHECTOMY AND WITH COMBINED ADRENALECTOMY-SYMPATHECTOMY IN THE TREATMENT OF PATIENTS WITH ESSENTIAL HYPERTENSION

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THE purpose of this presentation is to compare the results obtained following thoracolumbar sympathectomy and those obtained following combined adrenalectomy-sympathectomy in the treatment of patients with severe essential hypertension. It is apparent from our own experience and from the reported experiences of others that thoracolumbar sympathectomy is not a completely satisfactory type of therapy. It should be emphasized, however, that thoracolumbar sympathectomy is the only type of therapy for which data have been presented to show that the patients' lives have been extended over that observed in patients not treated surgically.[1, 2] Having subjected a number of patients to unilateral adrenalectomy in combination with thoracolumbar sympathectomy, four years and three months ago we subjected our first patient to bilateral resection of the adrenal glands. After a limited experience with subtotal adrenalectomy we began to combine bilateral subtotal adrenalectomy with a limited sympathectomy—a modified Adson sympathectomy. More recently a number of patients have had bilateral total adrenalectomy instead of a subtotal adrenalectomy (in combination with limited sympathectomy). It is our opinion that the more severely ill patients can withstand bilateral adrenalectomy and limited sympathectomy better than they can withstand extensive thoracolumbar sympathectomy. In addition, it has been our clinical impression that the patients who have had adrenalectomy-sympathectomy have had better results postoperatively. The present report must be considered as a preliminary comparison, since patients of the adrenalectomy-sympathectomy series have not been followed postoperatively as long as those of the thoracolumbar sympathectomy series.

The data to be presented are those of seventy-six patients subjected to extensive thoracolumbar sympathectomy followed from three to seven years

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and the data of 125 patients subjected to combined adrenalectomy-sympathectomy followed from zero to four years. The data of these two series of patients are reported in detail elsewhere.[2, 4] The specific follow-up data are listed only for surviving patients, except, of course, the survival rates. The patients are classified according to the severity of their disease preoperatively by the Smithwick grouping method.[1] For the purpose of this comparison the Smithwick groupings IV and V have been maintained. Recently Smithwick has not attempted to subdivide groups IV and V, simply indicating all such patients as group IV patients. Group V patients have a resting diastolic pressure of more than 140 mm. of Hg. Table I shows the number of patients and the percentage of patients in each series divided according to their Smithwick groupings. Of the patients subjected to adrenalectomy-sympathectomy, 18 per cent were in group IV, and 29 per cent were in group V, whereas among the patients subjected to thoracolumbar sympathectomy 22 per cent were in group IV and 29 per cent were in group V. The average Smithwick grouping of the patients subjected to adrenalectomy-sympathectomy was 3.5 and the average Smithwick grouping of the patients subjected to thoracolumbar sympathectomy was 3.6. Thus it can be said that the two series of patients were closely comparable with respect to the severity of disease preoperatively.

TABLE I. SMITHWICK CLASSIFICATION OF PATIENTS

SMITHWICK GROUP	ADRENALECTOMY-SYMPATHECTOMY PATIENTS	THORACOLUMBAR SYMPATHECTOMY PATIENTS
I	0 (0%)	2 (3%)
II	32 (26%)	19 (25%)
III	34 (27%)	16 (21%)
IV	22 (18%)	17 (22%)
V	37 (29%)	22 (29%)
Average grouping	3.5 (125 patients)	3.6 (76 patients)

The extent of resection of the sympathetic nerves in the two series of patients is shown in Fig. 1. The patients who were subjected to thoracolumbar sympathectomy had excision of the three splanchnic nerves and excision of the ganglionated sympathetic chain including the third lumbar ganglion and the ganglion corresponding to the highest gross origin of the greater splanchnic nerve. In most instances excision of the ganglionated chain included removal of the fifth or sixth thoracic sympathetic ganglion, although occasionally, the origin of the greater splanchnic nerve varied between the third and the eighth thoracic ganglia. When a combined adrenalectomy-sympathectomy was performed, approximately one inch of the greater and lesser splanchnic nerves was excised and the ganglionated sympathetic chain was excised from the twelfth thoracic to the second lumbar ganglia, inclusive. In approximately two-thirds of the patients a small fragment of adrenal gland was left in situ on one side, while in the remainder a total bilateral adrenalectomy was performed.

The average supine blood pressure for the 125 patients subjected to adrenalectomy-sympathectomy preoperatively was 209/125 mm. of Hg. The

average postoperative blood pressure of the patients surviving this operation (fourteen unknown) was supine 158/105 and standing 141/104. The average supine decrease in blood pressure of these individuals was, therefore, 51/20 mm. of Hg. On standing there was a further average decrease of 17 mm. of Hg in the systolic blood pressure.

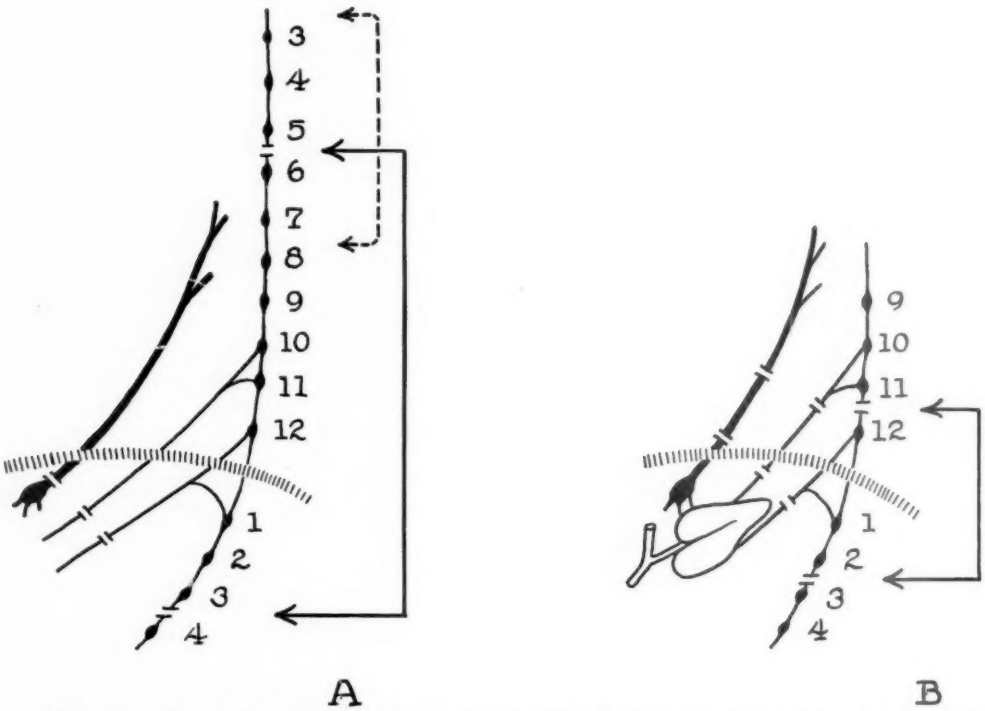

Fig. 1.—*A* shows the extent of resection in the individuals subjected to thoracolumbar sympathectomy. In general, the thoracic chain from the sixth thoracic to the third lumbar ganglia was removed together with the three splanchnic nerves.

B shows the extent of resection of the ganglionated sympathetic chain and segments of the splanchnic nerves when a combined adrenalectomy-sympathectomy was performed. In all cases one adrenal gland was removed completely, and in most of the cases a small fragment of the second gland was not removed. Recently, it has been the practice to perform a bilateral total adrenalectomy.

Of the patients subjected to thoracolumbar sympathectomy, the average preoperative supine blood pressure was 218/133 mm. of Hg. The average postoperative supine blood pressure of the living patients (six unknown) was 174/106 mm. of Hg. The average postoperative standing blood pressure of these patients was 151/105 mm. of Hg. Thus the patients subjected to thoracolumbar sympathectomy had an average blood pressure drop of 44/27 mm. of Hg. On standing, these individuals exhibited a further decrease in systolic blood pressure equivalent to 23 mm. The average postoperative blood pressure responses in the two series of patients were, therefore, similar.

For the purpose of tabulating the blood pressure response of the surviving individuals an arbitrary classification is used.[2, 4] As shown in Table II, 30 per cent of the patients subjected to thoracolumbar sympathectomy and 50

per cent of the patients submitted to adrenalectomy-sympathectomy had an "excellent" blood pressure response, or a blood pressure less than 150/100 supine and standing. Twenty-seven per cent of the adrenalectomy-sympathectomy group and 34 per cent of the thoracolumbar sympathectomy group had a "fair" blood pressure response—blood pressure from 155/100-180/110. A poor response or failure to respond was found in 22 per cent of the adrenalectomy-sympathectomy patients and in 36 per cent of the thoracolumbar sympathectomy patients.

TABLE II. BLOOD PRESSURE RESPONSES

BLOOD PRESSURE SUPINE AND STANDING	ADRENALECTOMY-SYMPATHECTOMY (%)	THORACOLUMBAR SYMPATHECTOMY (%)
Excellent, less than 150/100	50	30.1
Fair, 150/100—185/110	27.4	34
Poor, 180/110—200/120	14.3	25.3
Failure, more than 200/120	8.3	10.6

Tables III, IV, and V show the postoperative changes observed in electrocardiograms, heart size, and retinopathy. Although none of the patients have been lost to follow-up, these data are only 77 per cent to 90 per cent complete, as indicated in the detailed reports published elsewhere.[2, 4] Table III shows the changes in electrocardiograms. Of the patients subjected to adrenalectomy-sympathectomy 42.7 per cent had indications of improvement, 48.8 per cent showed no change, and 8.5 per cent showed evidences of further abnormalities. Of the patients subjected to thoracolumbar sympathectomy, the tracings were improved in 32.6 per cent, the same in 53.5 per cent, and worse in 13.9 per cent. Patients subjected to adrenalectomy-sympathectomy thus showed a greater tendency toward improvement in their electrocardiograms than did patients subjected to thoracolumbar sympathectomy.

Table IV shows the data of the two series of patients in regard to heart size preoperatively, and at the time of follow-up examination. A decrease in heart size indicates a definite and persistent decrease in frontal area or transverse diameter by orthodiagram in those individuals who were found to have definite cardiac enlargement preoperatively. Those individuals who had normal heart size or who had an increase in heart size preoperatively and who show no change in heart size postoperatively are listed as showing the same heart size. Of the surviving patients 68 per cent of the adrenalectomy-sympathectomy patients and 38 per cent of the thoracolumbar patients had cardiac enlargement preoperatively. The patients treated by adrenalectomy-sympathectomy had a greater percentage of decreases in heart size and fewer increases in heart size postoperatively than those treated by thoracolumbar sympathectomy.

Table V indicates the changes in ocular fundi or changes in retinopathy as observed in the surviving patients. Of the patients treated by adrenalectomy-sympathectomy, 55 per cent were improved, 43.7 per cent were the same,

and 1.3 per cent showed a progression of the pathologic changes. Of the patients treated by thoracolumbar sympathectomy, 58 per cent showed improvement of the eye grounds, 37 per cent were the same, and 5 per cent were worse.

TABLE III. CHANGES IN ELECTROCARDIOGRAMS

ELECTROCARDIOGRAM	ADRENALECTOMY-SYMPATHECTOMY (%)	THORACOLUMBAR SYMPATHECTOMY (%)
Improved	42.7	32.6
Same	48.8	53.5
Worse	8.5	13.9

TABLE IV. CHANGES IN HEART SIZE

HEART SIZE	ADRENALECTOMY-SYMPATHECTOMY (%)	THORACOLUMBAR SYMPATHECTOMY (%)
Decreased	41.7	31.8
Same	54.5	56
Increased	3.8	12.2

TABLE V. CHANGES IN OCULAR FUNDI

OCULAR FUNDI	ADRENALECTOMY-SYMPATHECTOMY (%)	THORACOLUMBAR SYMPATHECTOMY (%)
Improved	55	58
Same	43.7	37
Worse	1.3	5

As previously stated, it has been our impression that our combined adrenalectomy-sympathectomy is a less traumatic operative procedure than thoracolumbar sympathectomy. Table VI lists the postoperative complications and sequelae observed following the two-stage operations in the two series of patients during hospitalization or within a period of thirty days from the time of operation. The incidence of complications and sequelae in patients subjected to adrenalectomy-sympathectomy was 52.4 per cent per operation, and the incidence of complications and sequelae to patients in the thoracolumbar sympathectomy series was 82.9 per cent. In addition to having a lower incidence of complications per patient or a lower morbidity rate, the patients subjected to adrenalectomy-sympathectomy required a shorter period of hospitalization by several days and briefer period of anesthesia than required by the individuals subjected to thoracolumbar sympathectomy. Patients subjected to thoracolumbar sympathectomy have more persistent backache postoperatively than do patients subjected to adrenalectomy-sympathectomy. It is also our impression that patients with borderline renal function are better able to withstand adrenalectomy-sympathectomy than thoracolumbar sympathectomy.

Table VII shows the survival rates of the patients of the two series according to the Smithwick grouping method. There is a higher survival rate for Smithwick groups II, IV, and V patients treated by adrenalectomy-sympa-

thectomy. The survival rates include an operative mortality of 5 per cent for the adrenalectomy-sympathectomy series and 1.3 per cent for the thoracolumbar series.

TABLE VI. COMPLICATIONS AND SEQUELAE OCCURRING WITHIN THIRTY DAYS FOLLOWING OPERATION

	ADRENALECTOMY-SYMPATHECTOMY	THORACOLUMBAR SYMPATHECTOMY
Pleural effusion	8	43
Pneumothorax	8	16
Hemothorax	5	10
Hydropneumothorax	0	5
Pneumohemothorax	0	4
Atelectasis	4	5
Empyema	0	1
Bronchopneumonia	0	1
Acute pulmonary edema	0	1
Pleuritis	3	0
Pulmonary infarction (nonfatal)	3	2
Thrombophlebitis	11	8
Cardiac arrest	0	1
Coronary occlusion		
nonfatal	3	0
fatal	1	0
Cerebral vascular accident		
nonfatal	3	4
fatal	1	0
Azotemia	2	5
Wound infection and hematoma	12	1
Persistent fever	10	2
Significant hemorrhage		
nonfatal	9	0
fatal	1	0
Congestive heart failure		
nonfatal	2	0
fatal	1	0
Adrenal insufficiency	11	0
Miscellaneous	33	17
Total complications and sequelae	131	126
Total patients	125	76
Total operations	250	152
Incidence complications and sequelae per operation	52.4%	82.9%

TABLE VII. SURVIVAL RATES

SMITHWICK GROUP	ADRENALECTOMY-SYMPATHECTOMY 0-4 YEARS (%)	THORACOLUMBAR SYMPATHECTOMY 3-7 YEARS (%)
Group I	–	100
Group II	91	84
Group III	80	88
Group IV	86	59
Group V	62	50

SUMMARY

1. The zero- to four-year follow-up data of 125 patients subjected to adrenalectomy-sympathectomy and the three- to seven-year follow-up of seventy-six patients subjected to thoracolumbar sympathectomy are summarized.

2. The two series of patients are comparable with respect to the severity of their disease preoperatively. The patients subjected to adrenalectomy-sympathectomy had an average Smithwick grouping rating of 3.5, and those subjected to thoracolumbar sympathectomy 3.6.

3. A higher incidence of excellent blood pressure responses and a lower incidence of poor responses or failure to respond were found in the adrenalectomy-sympathectomy series.

4. The data indicate that the postoperative changes in the electrocardiographic tracings and heart size were more satisfactory in the adrenalectomy-sympathectomy series.

5. The operative morbidity was higher in the thoracolumbar sympathectomy series. The operative mortality was higher in the adrenalectomy-sympathectomy series.

6. Survival rates were superior following adrenalectomy-sympathectomy for the Smithwick groups II, IV, and V patients.

7. The present report is a preliminary one. It should be emphasized that the difference in the average follow-up period for both series of patients does not allow a firm and definite comparison.

REFERENCES

1. Smithwick, R. H.: Hypertensive Cardiovascular Disease, J. A. M. A. 147: 1611, 1951.
2. Zintel, H. A., Sellers, A. M., Jeffers, W. A., Mackie, J. A., Hafkenschiel, J. H., and Lindauer, M. A.: Results of Thoracolumbar Sympathectomy for Essential Hypertension: 3 to 7 Year Follow-Up of 100 Patients, Arch. Surg. To be published.
3. Smithwick, R. H.: Surgical Physiology of Hypertension, S. Clin. North America 9: 1699, 1949.
4. Zintel, H. A., Sellers, A. M., Jeffers, W. A., Mackie, J. A., Hafkenschiel, J. H., and Lindauer, M. A.: Thoracolumbar Sympathectomy in the Treatment of Severe Hypertension: 3 to 7 Year Follow-Up of 76 Patients. To be published.

THE EFFECT OF PREVIOUS LEVEL OF PROTEIN FEEDING ON WOUND HEALING AND ON METABOLIC RESPONSE TO INJURY

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INTRODUCTION

THE importance of protein nutrition in wound healing is widely recognized. Frank protein deficiency leads to delay in wound healing, but satisfactory healing is ultimately attained (see Levenson and associates[1] for review of literature). In the uninjured animal the size of the body stores of protein is influenced by the amount of protein in the diet. As the protein level of the diet is increased above that required for nitrogen equilibrium additional amounts of protein are stored, especially in the liver.[2] Because this extra protein storage induced by high protein feeding is readily reversed by caloric restriction, starvation,[2, 3] or injury,[4] it has come to be designated as "labile" protein stores. Conversely the magnitude of the catabolic response to injury, in regard to nitrogen loss, is proportional to the size of the "labile" protein stores and therefore to the preinjury plane of protein feeding. The question presents itself as to whether this metabolic variation in response to injury induced by differences in preinjury protein feeding is associated with differences in wound healing. It was therefore undertaken in this study to compare the response to injury of animals previously fed minimal or liberal levels of dietary protein.

METHODS

Male albino rats were fed a commercial stock diet until 250 to 300 grams of body weight was attained. The animals were then divided into three groups and, for two weeks, fed purified diets which varied only in the amount of protein supplied: one, two, or three times the minimum requirement for nitrogen equilibrium (53 mg. nitrogen per 100 grams of body weight per day[5]). The protein source was casein supplemented with methionine, 30 mg. per gram of protein, incorporated at levels 10.45 per cent to 31.34 per cent of the diet. Other diet components were: vitamin-supplemented corn oil,* 10 per cent; U.S.P. salts No.

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*Containing 0.01 per cent halibut liver oil and 0.003 per cent α tocopherol.

2, 4 per cent; B vitamin mixture,* 1 per cent; and sucrose 53.66 per cent to 74.55 per cent. Forty-eight calories was offered per day, which was sufficient to maintain body weight essentially constant, and the feeding period was limited to seven hours. Urine and feces were collected during the last two days of this period for measurement of nitrogen balance.

On the fifteenth day five control animals from each group were sacrificed and the remainder subjected to injury. The animals to be injured were first anesthetized with sodium pentobarbital and shaved. A 4 cm. midline abdominal incision was then performed and the wound closed by interrupted, through-and-through, No. 34 steel sutures at 1 cm. intervals. A 5 cm. shaved dorsal area, immediately anterior to the transverse process of the sacrum, was marked and the animal burned within the demarcated space by immersion for fifteen seconds in water heated to 90° C., a slight modification from the procedure of McCarthy.[6] The incision served as a means of quantitating wound healing; the burn was added as a further metabolic stress. Levenson and co-workers[7] found that incised wounds healed more slowly in burned animals than in unburned controls.

No food was given on the day of injury, but ad libitum water intake was permitted. During the recovery period the groups prefed one or three times the protein requirement were divided, one half of the animals continuing on the same diet and one half receiving two times the protein requirement. This arrangement, as shown in Table I, provided three groups which differed only in the diet fed before injury and three groups in which the diet pattern was unchanged but at varying levels. On the first day after injury two-thirds of the previous food intake was offered, and during the remainder of the recovery period the standardization allowance was supplied, 48 calories per day. Urine collections were made over two-day periods beginning with the day of injury and continuing to the tenth day postinjury. Five or six animals from each group were sacrificed on the fourth, seventh, and tenth postinjury days.

TABLE I. NITROGEN CONTENT OF FOOD

	NITROGEN ALLOWANCE			
	STANDARDIZATION		POSTINJURY	
GROUP	MG./DAY	% OF REQUIREMENT	MG./DAY	% OF REQUIREMENT
1-1	162	100	162	100
1-2	162	100	315	200
2-2	315	200	315	200
3-3	475	300	475	300
3-2	475	300	315	200

At sacrifice, the abdominal wound, burned area, liver, and adrenals were excised. One half of the wound was preserved for histologic examination and the remainder used for measurement of tensile strength as follows: A 1 cm.

*Supplying per 100 Gm. of diet:

thiamine hydrochloride	0.50 mg.	p-aminobenzoic acid	5.00 mg.
riboflavin	0.50 mg.	biotin	0.01 mg.
pyridoxine hydrochloride	0.25 mg.	folic acid	0.10 mg.
nicotinamide	2.00 mg.	vitamin K	0.10 mg.
calcium pantothenate	2.00 mg.	choline chloride	100.00 mg.
inositol	10.00 mg.	vitamin B_{12}	50 μg

strip was cut at suture lines and suspended from a screw clamp parallel to the incision. A second clamp to which was attached a paper container was fastened at the opposite end while supported from below, so that no weight was borne by the tissue. The support was then removed and lead shot added at a constant rate until the wound separated. The tensile strength was the combined weight of clamp plus container plus shot. The procedure was carried out on two strips from each wound (one from each end) and the average value used for comparisons.

The burns were inspected for estimation of necrosis, ulceration, and suppuration and the area traced on acetate film. The tracing was cut out and weighed and the area of the burn calculated from the weight of a known area of the acetate film. The body surface area of the animal was calculated from the formula derived by Mitchell[8]: body surface area, sq. cm. = 13.2 weight.$^{0.64}$ Burn size was then expressed as a percentage of body surface. A representative portion of the burn was reserved for histologic examination.

The adrenals were cleaned and weighed immediately. The livers were weighed and analyzed for moisture, nitrogen, and fat.[9]

The methods used for staining and examining the slides of the wounds were those described in detail by Pirani, Stepto, and Sutherland.[10]

The wound sections were examined in a uniform manner without previous knowledge of the origin of the slide. The wound area was arbitrarily defined as that limited by the epidermis and the peritoneal surface in one direction and by the width of two low-power (X35) fields on the other. Each specific histologic detail being investigated was then graded in arbitrary units (1+ to 4+) and tabulated in an attempt to obtain a quantitative evaluation of the possible changes. The general appearance, as well as the cellular features of the wounds, were studied in the slides stained with hematoxylin and eosin. Collagen fibers were stained by the van Gieson technique.[11] As the collagen fibers are formed and mature, they gradually vary in color from pale pink to brilliant red, while immature collagen stains uniformly yellow. Toluidine blue for mucopolysaccharides was used in a 1:1,000 aqueous solution at pH 4.25 for one minute.[12] After staining, the section was washed in distilled water for twenty seconds, blotted dry with filter paper, and mounted in crown oil. The slides were read within five minutes. The leukofuchsin periodic acid method for glycoprotein[13] disclosed leukofuchsin-reacting material in small amounts distributed throughout the wound granulation tissue and within mast cells.

RESULTS AND DISCUSSION

Body Weight and Food Consumption.—At the end of standardization the body weight of the group fed the minimal protein level (270 grams) was significantly lower than that of the other two groups (279 grams) ($F = 13.13$, $P<0.01$). On the day of wounding the differences between the subgroups within each level of preinjury protein feeding were not significant ($F<1$).

The mean body weight loss between the day of wounding and the day of sacrifice was 10.2 grams at PI 4 (postinjury day 4), 11.7 grams at PI 7, and 12.5

grams at PI 10. These differences are not significant ($F = 1.29$, $P > 0.05$). Nor were there significant differences in weight loss among the five postinjury diet groups ($F = 1.89$, $P > 0.05$). The body weight fell sharply in the first two postinjury days, rose somewhat in the next two days, and then remained relatively constant.

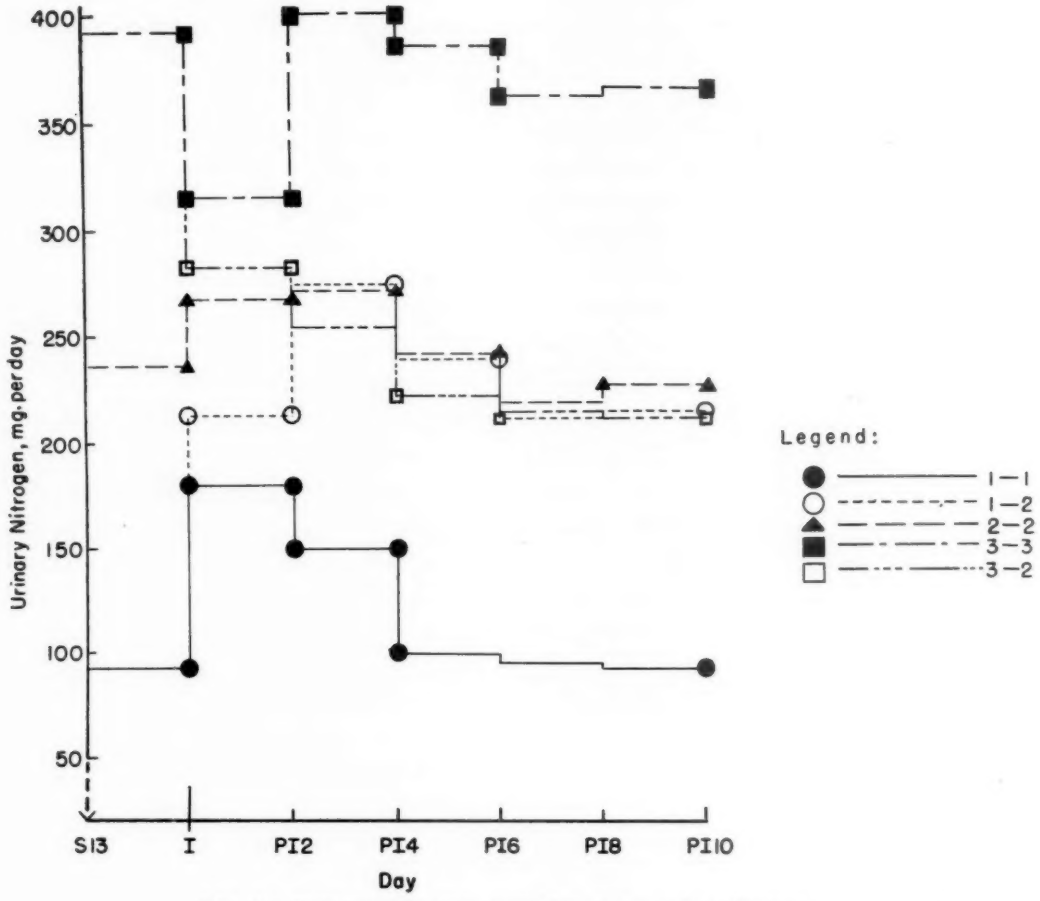

Fig. 1.—Urinary nitrogen excretion pre- and postinjury.

The total caloric intake between the day of injury and the day of sacrifice did not differ significantly between the various diet groups (PI 4, $F < 1$; PI 7, $F = 1.42$; PI 10, $F < 1$). In the PI 10 subgroups used for nitrogen excretion measurement throughout, slight variation in food consumption was noted and is discussed in connection with nitrogen balance.

Urinary Nitrogen Excretion and Nitrogen Balance (Figs. 1, 2, and 3).—During the last two days of the period of standardization all groups were in positive nitrogen balance and there were no significant differences between groups in this regard. When the minimum protein requirement was met, 56 mg. of nitrogen was retained per day; at two or three times requirement, daily retentions were 62 mg. to 64 mg. Virtually all the additional nitrogen fed was excreted in the urine, the daily excretion rising from 92 mg. to 236

mg. to 392 mg. with increasing intake (Fig. 1). The wasteful nature of the excess feeding is best expressed by converting the nitrogen retentions to percentage of that absorbed, giving values of 38 per cent, 21 per cent, and 14 per cent at one, two, and three times the requirement, respectively.

The pattern of urinary nitrogen excretion is shown in Fig. 1. On the day of injury and the first day following, nitrogen excretion of the groups prefed the minimum requirement (1-1 and 1-2) rose markedly above the preinjury level. Those animals prefed double the requirement (2-2) exhibited only a slight rise in nitrogen excretion, and those previously maintained at three times requirement (3-3 and 3-2) excreted less than during the control period.

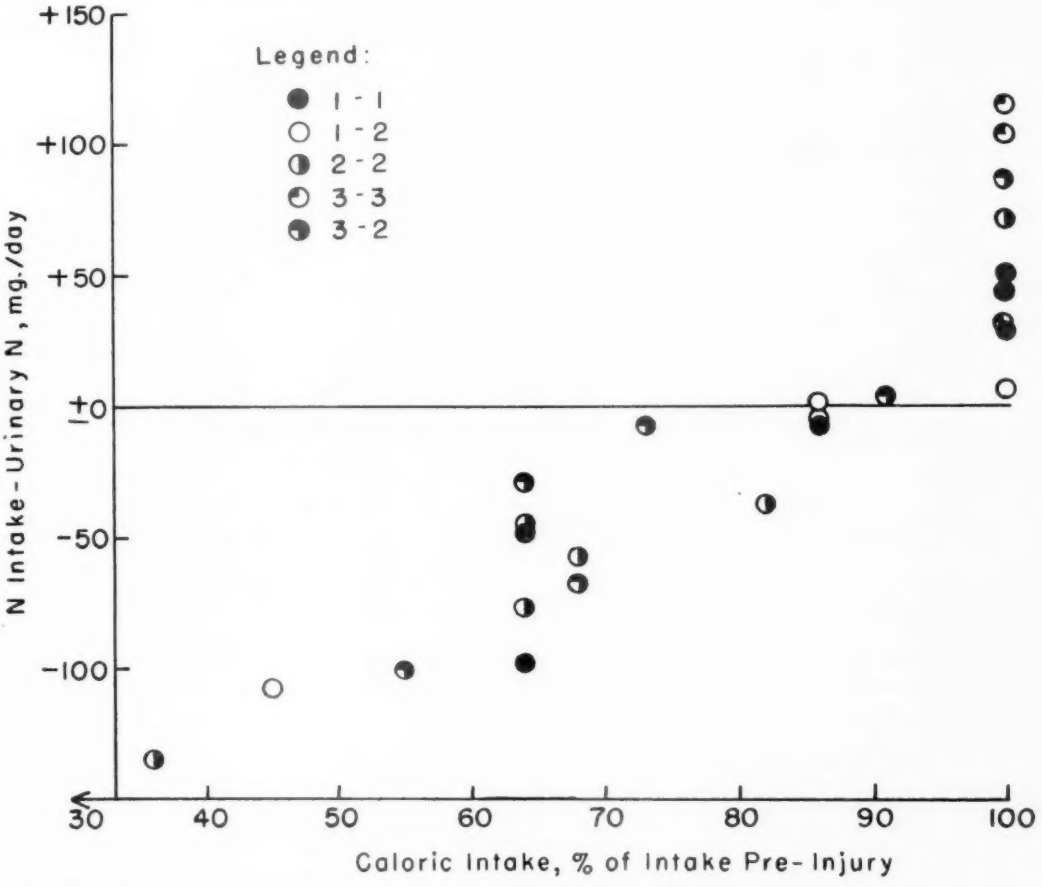

Fig. 2.—Relationship between food intake and nitrogen balance at the second and third days after injury.

During the next period the results were confounded by incomplete food consumption but three distinct levels of excretion related to intake were apparent. By the fourth and fifth days after injury excretions approximated those obtained before injury and remained essentially constant thereafter. The group continued at the minimum protein level returned to excretions identical with those found during standardization, but excretions at two or three times

minimal requirement were slightly less than previously observed. The catabolic response to injury cannot be accurately assessed because the food intake in the immediate postinjury period was less than during the standardization

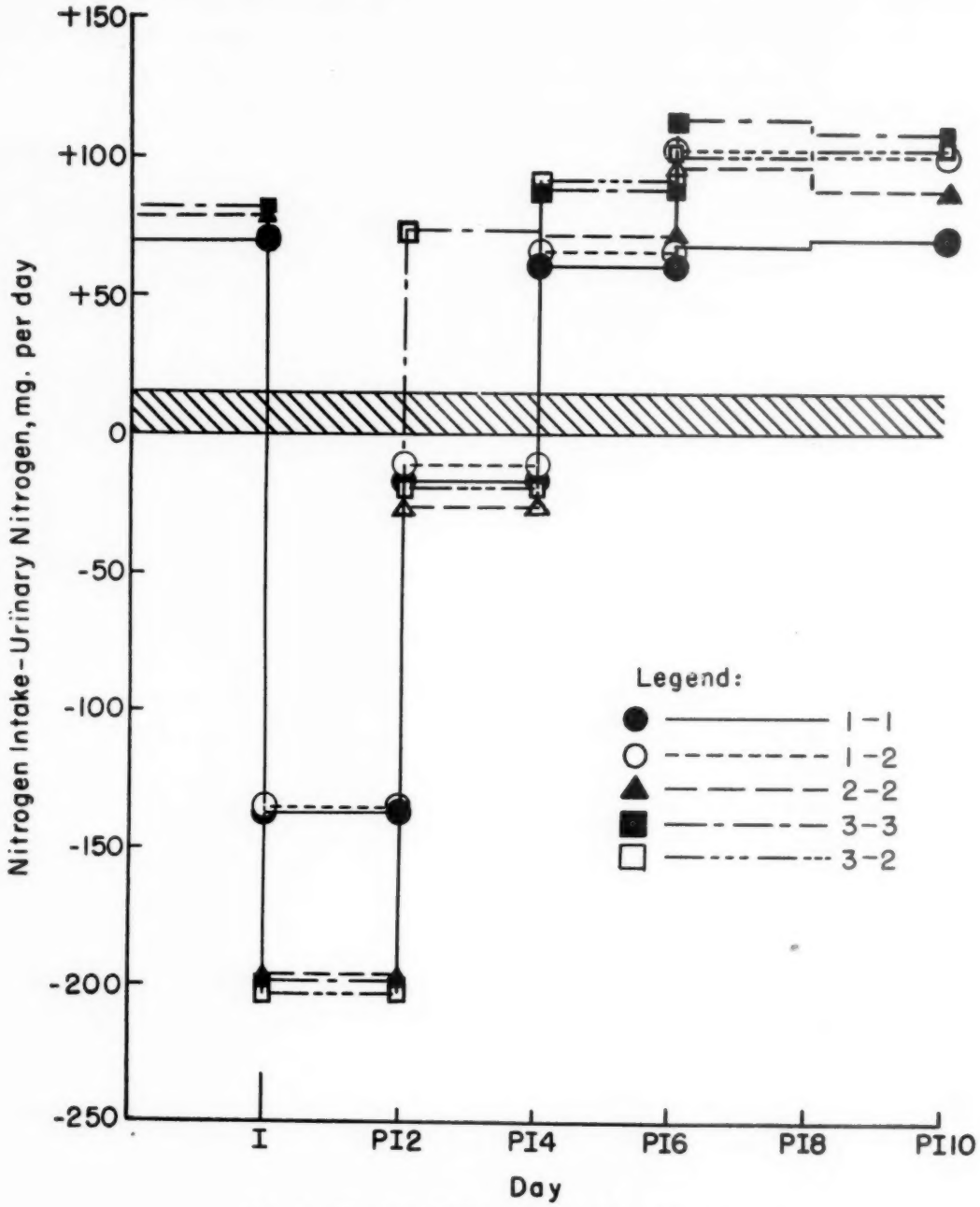

Fig. 3.—Nitrogen "balance" pre- and postinjury.

period, so that the effects of decreased food intake and response to injury were confounded. The total catabolic response to these two effects, as reflected by negativity of nitrogen balance, will be considered presently. However, by the

time food intake had returned to the standardization level (PI 4 and 5) nitrogen excretion was not greater than during standardization. Therefore, the catabolic response to injury, if present, had ended by this time.

The marked effect of food intake on nitrogen balance, during the second and third days after injury, is demonstrated in Fig. 2. Regardless of protein supplied, nitrogen balance was negative unless the food intake, and hence caloric intake, was above 85 per cent of that required to maintain body weight before injury. Comparisons between groups during the second and third days after injury could not be made because of this variation in food consumption. Only the animals given the highest protein level ate the total food allowance during this period, and they were in positive balance.

Immediately following injury the groups prefed two or three times the minimum requirement were in more negative nitrogen balance than were those on minimal allowance: –200 mg. per day as opposed to –137 mg. per day ($F = 29.55$, $P < 0.01$). The difference between the group prefed twice the minimal nitrogen requirement and the groups prefed three times this level was not significant ($F < 1$). From the fourth day postinjury on, all groups were in positive nitrogen balance and those fed the luxus levels of protein retained more nitrogen (95 mg. per day) than the low-protein group (65 mg. per day) ($F = 18.78$, $P < 0.01$), but the difference between the groups on two and three times minimal requirement was not significant ($F = 3.76$, $P > 0.05$). On the higher-protein diets greater retention of nitrogen was attained during recovery than preinjury ($F = 5.56$, $P < 0.05$), but retention of the lower-protein diet was unchanged. The nitrogen balance of the 1-2 group was significantly greater than that of the 1-1 group ($F = 8.07$, $P < 0.01$), but the retention of the 3-2 group was not significantly greater than that of the 1-2 group ($F = 1.25$, $P > 0.05$), nor was that of the 3-3 group superior to that of the 3-2 group ($F < 1$). It would appear, from the standpoint of nitrogen balance, that the most efficient scheme of feeding was the minimum requirement before injury with an increased intake to double the requirement during recovery. The positivity of balance rose significantly in all diet groups between PI 4 and 5 and PI 6 and 7 ($F = 23.33$, $P < 0.01$) but did not change significantly between PI 6 and 7 and PI 8 and 9 ($F < 1$).

Liver Weight and Composition (Tables II and III).—At the end of standardization the means of the wet weight of the liver did not differ significantly among the groups in the experiment as a whole ($F < 1$). In the postinjury period mean wet weight of the liver did not differ significantly among the diet groups ($F < 1$) or among the groups sacrificed on various days ($F = 2.305$, $P > 0.05$). Similarly the total water content of the liver did not differ among diet groups at the end of standardization ($F < 1$) or in the postinjury period among diet groups ($F < 1$) or among groups sacrificed on various days ($F = 2.72$, $P > 0.05$). However, the wet weight of the liver and percentage of water increased slightly in all groups after injury. Only in the

groups prefed triple the protein requirement were these increases significant ($P < 0.01$), and the increase in weight was accountable to the increase in total water content.

TABLE II. LIVER WEIGHT AND MOISTURE CONTENT

GROUP	1-1	1-2	2-2	3-3	3-2
Wet weight					
control, grams	14.33		14.68	13.60	
PI 4, grams	14.96	14.78	14.98	16.10	15.07
PI 7, grams	13.79	14.80	14.44	14.45	14.31
PI 10, grams	13.99	14.85	14.35	15.13	15.44
Moisture					
control, %	72.4		70.1	69.8	
total, grams	10.37		10.32	9.49	
PI 4, %	74.0	73.7	73.2	73.0	73.0
total, grams	11.07	10.90	10.97	11.75	11.00
PI 7, %	72.7	73.6	72.8	73.2	72.9
total, grams	10.1	10.91	10.52	10.59	10.42
PI 10, %	73.4	73.4	72.8	72.6	73.3
total, grams	10.27	10.89	10.44	10.98	11.33

TABLE III. LIVER NITROGEN AND FAT CONTENT

GROUP	1-1	1-2	2-2	3-3	3-2
Nitrogen					
control, %*	11.41		11.70	12.04	
total, mg.	451		510	494	
PI 4, %	12.06	12.49	12.19	12.55	12.35
total, mg.	469	484	490	545	502
PI 7, %	12.37	12.71	12.72	12.74	12.73
total, mg.	467	496	499	492	494
PI 10, %	11.63	12.53	12.31	12.55	12.25
total, mg.	432	496	481	520	510
Fat					
control, %*	8.16		8.81	8.18	
total, mg.	321		384	337	
PI 4, %	8.30	7.31	8.39	7.00	7.82
total, mg.	322	283	332	305	315
PI 7, %	7.79	6.83	7.17	7.51	6.90
total, mg.	293	266	282	286	266
PI 10, %	8.49	7.29	7.54	7.16	7.87
total, mg.	313	290	294	297	328

*Dry weight basis.

The total nitrogen content of the liver at the end of standardization was higher in the groups receiving two or three times the minimal requirement than in the group receiving the minimal level ($F = 4.24$, $P < 0.05$). In the postinjury period the differences attributable to day of sacrifice were not significant ($F < 1$). The liver nitrogen content of the 1-1 group was significantly lower ($F = 9.31$, $P < 0.01$) and of the 3-3 group significantly higher ($F = 5.26$, $P < 0.05$) than those of the other groups, indicating that the extremes of levels of protein feeding were reflected in liver nitrogen stores during recovery.

The total fat content of the liver did not differ significantly among the diet groups at the end of standardization ($F = 3.58$, $P > 0.05$), nor did the diet groups differ significantly in the postinjury period ($F = 1.69$, $P > 0.05$).

However, the liver fat content in the postinjury period was significantly lower than at the end of standardization in all diet groups ($F = 26.73$, $P < 0.01$). In each diet group the lowest liver fat content occurred on the seventh day postinjury, and the value for this day differed significantly from the PI 4 and PI 10 values ($F = 13.37$, $P < 0.01$), but the PI 4 and PI 10 values did not differ significantly ($F < 1$).

Adrenal Weight (Table IV).—There were no significant differences in adrenal weights prior to injury between groups fed the different protein levels ($F < 1$). Adrenal hypertrophy occurred in all groups during the postinjury period ($F = 37.09$, $P < 0.01$). During the postinjury period the differences between days of sacrifice ($F < 1$) and between diets ($F = 1.05$, $P > 0.05$) were not significant, but the diet-days interaction was highly significant ($F = 3.14$, $P < 0.01$). This indicates that the pattern of change in adrenal weight in the course of the postinjury period varied greatly among the diet groups, as is evident from the data. Thus groups 1-1, 3-3, and 3-2 showed the greatest adrenal size by PI 4, whereas in groups 1-2 and 2-2 this occurred on PI 10, at which time the adrenals of the other groups had returned to nearly normal size. This pattern does not suggest any simple relationship between the time course of adrenal enlargement after injury and the level of protein feeding before or after injury.

TABLE IV. ADRENAL WEIGHT

GROUP	1-1	1-2	2-2	3-3	3-2
Control, mg./100 grams BW*	15.3		16.2	16.5	
PI 4, mg./100 grams BW	20.6	18.0	17.9	19.9	19.2
PI 7, mg./100 grams BW	17.5	18.2	19.5	19.8	18.9
PI 10, mg./100 grams BW	17.2	19.6	19.9	18.2	17.9

*Body weight.

Under certain experimental conditions high-protein feeding has been found to lead to adrenal hypertrophy.[14] In the present study the enlargement of the adrenals may reasonably be ascribed to the injuries acting as stressor agents.[15] The cause of the difference in time course of this adrenal hypertrophy among the diet groups is not apparent.

Burn Size (Table V).—The area of the burn, expressed as per cent of body surface area, did not differ significantly among the diet groups ($F < 1$). There was, however, a highly significant variation in burn size on the various postinjury days ($F = 9.21$, $P < 0.01$) which was entirely attributable to the low value on PI 7 since the values on PI 4 and PI 10 did not differ significantly ($F = 1.81$, $P > 0.05$). This decrease in burn size in the intermediate period can reasonably be attributed to cicatricial contraction.

TABLE V. BURN, PER CENT BODY SURFACE AREA

GROUP	PI 4	PI 7	PI 10
1-1	6.3	5.2	6.1
1-2	7.6	5.2	6.5
2-2	7.6	5.2	6.6
3-3	6.8	5.2	6.7
3-2	6.7	5.6	6.2

In order to determine whether the variation in burn size had a significant effect on the tensile strength of the wounds, an analysis of covariance was made, using the burn size as the covariate and the tensile strength as the variate. A test for reduction of error mean square of the tensile strength values due to regression on burn size gave an F value of less than 1 (not significant). In the 15 subgroups the correlation coefficient between burn size and tensile strength was statistically significant in only one, and an F test for differences among subgroups in regression of the variate on the covariate gave a value of less than 1 (not significant). On the basis of these analyses it was concluded that within the range of burn size encountered in this study there was no correlation between burn size and tensile strength of the wound.

Tensile Strength of Wounds (Table VI).—The differences between the tensile strengths of the wounds among the various diet groups were not significant ($F < 1$). Considering only the groups sacrificed on the fourth day postinjury, comparison of the two groups standardized at minimal protein requirement (mean tensile strength 56 Gm.) with the other 3 groups (mean tensile strength 84 Gm.) does not reveal a significant difference either when this comparison is made from the over-all analysis of variance ($F < 1$) or when a separate analysis of variance is made for the fourth postinjury day alone ($F = 3.91$, $P > 0.05$). Similarly in separate analyses of variance for the seventh postinjury day ($F < 1$) and the tenth postinjury day ($F = 1.79$, $P > 0.05$) the differences between diets are not significant. The mean tensile strength of all diet groups rose from 73 Gm. on PI 4 to 322 Gm. on PI 7 and 445 Gm. on PI 10. In the over-all analysis of variance the differences between postinjury days are highly significant ($F = 157.55$, $P < 0.01$) and the individual differences between PI 4 and PI 7 and between PI 7 and PI 10 are also highly significant.

TABLE VI. WOUND TENSILE STRENGTH (MEANS AND STANDARD DEVIATIONS)

GROUP	PI 4 (GM.)	PI 7 (GM.)	PI 10 (GM.)
1-1	59 ± 34	372 ± 42	491 ± 124
1-2	53 ± 37	327 ± 97	520 ± 160
2-2	90 ± 39	323 ± 107	365 ± 94
3-3	86 ± 35	301 ± 61	417 ± 38
3-2	78 ± 31	296 ± 45	429 ± 56

In summary, no effect of protein level in the diet before injury or after injury on the tensile strength of the wound was observed.

Wound Histology.—The mean values of the scores obtained by histologic grading of the wounds are given in Table VII. In no instance are the differences between dietary groups significant. The hematoxylin and eosin and van Gieson stains gave steadily rising scores in all groups as the number of days postinjury increased, thus showing good correlation with the tensile strength measurements. The toluidine blue and leukofuchsin methods for mucopolysaccharides and glycoproteins showed decreasing intensity of staining with maturation, as has previously been reported by Pirani and associates.[10]

TABLE VII. MEAN SCORES OF WOUNDS GRADED HISTOLOGICALLY

STAIN	VAN GIESON			TOLUIDINE BLUE			LEUKOFUCHSIN		
POSTINJURY DAY	PI 4	PI 7	PI 10	PI 4	PI 7	PI 10	PI 4	PI 7	PI 10
Diet group									
1-1	1.6	2.6	4.0	3.2	2.2	1.0	2.2	2.0	1.0
1-2	1.2	2.5	4.0	3.4	2.8	1.2	2.0	2.3	1.0
2-2	1.8	2.8	3.5	2.2	1.6	1.8	1.2	1.7	1.2
3-3	1.4	3.0	4.0	2.7	1.7	1.0	1.8	1.7	1.2
3-2	1.4	2.5	3.8	3.2	2.0	2.0	1.3	1.7	1.2

The burns were examined histologically after staining with hematoxylin and eosin. No important differences between dietary groups were noted.

SUMMARY

Protein was fed to male rats at levels corresponding to one, two, or three times the minimum requirement (160, 320, or 480 mg. N per day) with calories sufficient to maintain body weight at 300 grams. These intakes in fourteen days produced uniformly positive nitrogen balance. At the end of this standardization period controls were sacrificed and the remaining animals subjected to a dorsal burn and a 4 cm. laparotomy. Recovery was followed for ten days, during which the groups were subdivided so that in each series one group was fed the same diet as during standardization and a second group the intermediate nitrogen level. Animals were killed on the fourth, seventh, and tenth postinjury days. Metabolic response was evaluated by urinary nitrogen excretion, liver composition, and adrenal weight and wound healing by tensile strength measurement and histologically.

None of the criteria employed detected significant alterations due to the level of protein fed prior to injury, except urinary nitrogen excretions and liver nitrogen content. In the groups prefed the minimal protein level, urinary excretion and hence negativity of nitrogen balance were less on the day of injury and first recovery day than in groups prefed the higher levels. The liver nitrogen content was higher at the end of the standardization period in the groups receiving the higher protein intakes than in the group receiving the minimal level.

During the recovery period, feeding higher levels of protein resulted in more positive nitrogen balance and greater total liver nitrogen content than did feeding the minimum requirement, but increasing the level from two to three times requirement afforded no further advantage. There were no other differences attributable to variation in protein intake after injury.

There were no significant differences attributable to level of protein feeding before or after injury in the tensile strength or histologic grading of the wounds.

CONCLUSIONS

It is concluded that maintenance of a high plane of protein nutrition before injury is without obvious benefit to the animal in terms of wound healing as compared with minimal, adequate nutrition.

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REFERENCES

1. Levenson, S. M., Birkhill, F. R., and Waterman, D. F.: The Healing of Soft Tissue Wounds; the Effects of Nutrition, Anemia, and Age, SURGERY **28:** 905, 1950.
2. Kosterlitz, H. W.: The Effects of Changes in Dietary Protein on the Composition and Structure of the Liver Cell, J. Physiol. **106:** 194, 1947.
3. Calloway, D. H., and Spector, H.: Influence of Standardizing Diet on Nitrogen Metabolism During Caloric Restriction, Fed. Proc. **12:** 410, 1953.
4. Munro, H. N., and Chalmers, M. I.: Fracture Metabolism at Different Levels of Protein Intake, Brit. J. Exper. Path. **26:** 396, 1945.
5. Goettsch, M.: Minimum Protein Requirement of the Adult Rat for 28 Day Periods of Maintenance of Body Weight, J. Nutrition **45:** 609, 1951.
6. McCarthy, M. D.: A Standardized Back Burn Procedure for the White Rat Suitable for Study of the Effects of Therapeutic and Toxic Agents on Long-term Survival, J. Lab. & Clin. Med. **30:** 1027, 1945.
7. Levenson, S. M., Pirani, C. L., Braasch, J. W., and Waterman, D. F.: The Effect of Thermal Burns on Wound Healing. Medical Nutrition Laboratory Report No. 117, Oct. 20, 1953.
8. Mitchell, H. H.: An Estimation of the Surface Area of the White Rat, Am. J. Physiol. **76:** 380, 1926.
9. Association of Official Agricultural Chemists: Official and Tentative Methods of Analysis, Washington, 1950. (Nitrogen, paragraph 2.22; fat, paragraph 13.19.)
10. Pirani, C. L., Stepto, R. C., and Sutherland, K.: Desoxycorticosterone Acetate and Wound Healing, Medical Nutrition Laboratory Report No. 75, 1951.
11. Lillie, R. D.: Histopathologic Technic, Philadelphia, 1948, The Blakiston Company, pp. 190-191.
12. Idem: p. 63.
13. Hotchkiss, R. D.: A Microchemical Reaction Resulting in the Staining of Polysaccharide Structures in Fixed Tissue Preparations, Arch. Biochem. **16:** 131, 1948.
14. Dontigny, P., Hoy, E. C., Prado, J. L., and Selye, H.: Hormonal Hypertension and Nephrosclerosis as Influenced by Diet, Am. J. M. Sc. **215:** 442, 1948.
15. Selye, H.: Physiology and Pathology of Exposure to Stress, Montreal, 1950, Acta Press.

BILATERAL HERNIOTOMY IN INFANTS AND CHILDREN

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IT HAS been recognized for many years that infants and children have a particularly high incidence of bilateral indirect inguinal hernia. Potts, Riker, and Lewis[1] mentioned that 20 per cent of inguinal hernias in infants are bilateral and 17 per cent are bilateral in older children. Iason[2] stated that 25 per cent of patients with oblique inguinal hernia on one side will eventually develop an indirect inguinal hernia on the other side. Although Gross[3] acknowledged the frequency of bilateral inguinal hernia in infants and children, he does not believe that it occurs with sufficient frequency to warrant routine bilateral surgical exploration. Dunavant and Wilson[4] could find bilateral inguinal hernia in only 4 per cent of some 250 infants and children on clinical examination preoperatively. The variations in statistical findings are, in all probability, occasioned by the fact that the diagnosis of inguinal hernia in infants and young children cannot always be made accurately on history or physical examination. A small hernia sac, or even a large one without omental or intestinal contents, often escapes detection by the examining finger.

During 1952, we operated on six children for indirect inguinal hernia upon whom we had operated for a hernia of the opposite side within the three previous years. At the time of the original herniotomy, there had been no clinical evidence that the lesion was bilateral. These findings led to the suspicion that a bilateral herniation existed in a large proportion of other cases in which only a one-sided operation had been carried out. It was felt, therefore, that surgical exploration of both inguinal regions was warranted routinely for all infants and children with clinical unilateral hernia. If this procedure were followed, it was thought that many patients might be spared a second period of hospitalization, a second anesthesia, and a second surgical procedure. Accordingly, during 1953 and 1954, fifty infants and children with preoperative clinical findings of unilateral inguinal hernia were subjected to bilateral surgical exploration. If there was the slightest suggestion of a bilateral hernia preoperatively, or if there was an accompanying hydrocele or undescended testicle, the case was excluded from the study.

In our series of cases, there were 47 boys and 3 girls, ranging in age from 1 month to 12 years. Twelve children were under 1 year of age, eleven children were between 1 and 4 years of age, nine children ranged in age from 4 to 6 years, ten children were 6 to 8 years of age, and eight children were between 8 and 12 years old. (See Table I.)

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TABLE I

AGE RANGES	NUMBER OF PATIENTS
1 month to 1 year	12
1 year to 4 years	11
4 years to 6 years	9
6 years to 8 years	10
8 years to 12 years	8
Total	50

The clinically palpable hernia was located on the right side in 33 patients and on the left side in 17 patients. A left-sided hernia was discovered on operative exploration in 25 of the 33 patients in whom only a right-sided hernia could be diagnosed preoperatively. A right-sided hernia was discovered on operative exploration in 12 of 17 patients on whom only a left-sided hernia could be diagnosed preoperatively. Thus, a contralateral hernia was demonstrated in 37 of 50 patients, or in 74 per cent of all cases. (See Table II.)

TABLE II

	NUMBER OF CASES	CONTRALATERAL HERNIA FOUND AT OPERATION	PER CENT WITH CONTRALATERAL HERNIA
Right-sided hernia on preoperative examination	33	25	75.7
Left-sided hernia on preoperative examination	17	12	70.6
Total	50	37	74.0

All patients were operated on under general anesthesia through small inguinal incisions which were carried down to the external oblique fascia. The external inguinal ring was incised for a distance of 1 to 2 cm., the cremaster muscle was split longitudinally, and the spermatic cord was explored carefully for the presence of a hernia sac. The incision of the external oblique fascia was an important maneuver as it permitted more thorough examination of the cord as it emerged from the internal inguinal ring. Often, a large portion of the sac would be found to lie in this region of the cord and if the external fascia had not been incised, it might have been overlooked. In addition, many of the smaller sacs may be obscured from view in their distal extremity by a small pad of fat tissue which is present in the area just beyond the external ring. When a hernia sac was located, it was picked up with a forceps and dissected free without disturbing the surrounding cord structures. The sac was twisted, doubly ligated with fine silk sutures, and amputated as high as possible. One or two fine, black silk sutures were inserted to approximate the incised external oblique fascia. No attempt was made in any of these cases to perform a plastic repair upon the muscle or fascial wall of the inguinal canal.

Because it is known that a process or extension of peritoneum can be demonstrated in practically all infants and young children at the level of the internal inguinal ring, no peritoneal protrusion of less than 2 cm. in length was considered to be a hernia. The length of the sacs on the "uninvolved" side was measured in all cases with the results as shown in Table III.

TABLE III. SIZE OF HERNIAL SACS ON SIDE WHERE NO HERNIA WAS DIAGNOSED PREOPERATIVELY

LENGTH OF SAC	NUMBER OF CASES
2 cm.	14
3 cm.	13
4 cm.	4
5 cm.	4
6 cm.	2
Total	37

It is interesting to note that the two children with the largest undiagnosed sacs, 6 cm. each, had smaller herniations on the side which was diagnosed clinically. All the sacs were opened and found to communicate freely with the peritoneal cavity, thus precluding the possibility that they were merely obliterated funicular processes. The failure to detect these herniations clinically can be explained by the fact that none of the sacs was found to have any contents.

All twelve of the patients under 1 year of age were found to have bilateral hernias. The hernias on the undiagnosed side appeared to be exceptionally large in this age group with two infants having 5 cm. sacs, two having 4 cm. sacs, and five infants having sacs of 3 cm. in length. These findings might indicate that there is a tendency for the sacs to decrease in size or actually become obliterated as the infant matures.

In the 1- to 4-year age group, 7 children were found upon operation to have bilateral hernias whereas 4 children had a hernia on one side only. In the 4- to 6-year age group, 8 or 9 children had bilateral hernias. In the 6- to 8-year age group, 5 of 10 children had both sides involved. In the 8- to 12-year age group, 5 to 8 children were found to have bilateral lesions. (See Table IV.)

TABLE IV. BILATERAL HERNIAS ACCORDING TO AGE GROUP

AGE GROUP	NUMBER OF CASES	NUMBER OF CASES WITH BILATERAL HERNIA	PER CENT
1 month to 1 year	12	12	100.0
1 to 4 years	11	7	63.6
4 to 6 years	9	8	88.8
6 to 8 years	10	5	50.0
8 to 12 years	8	5	62.5
Total	50	37	74.0

COMMENT

It is an accepted anatomic fact that congenital hernias are caused by failure of obliteration of the processus vaginalis. According to Zimmerman and Anson,[5] a large percentage of these open processes close spontaneously during the first few months of life but rarely close spontaneously after 6 months of age. Our operative findings would seem to bear out this contention as a contralateral defect was found in the older children in only 65.8 per cent of cases as compared to the 100 per cent which were found in the infants under 1 year of age. However, our studies reveal that a much larger number of infants and children in all age groups have hernias than can be discovered

on clinical examination. Operative findings indicate that when a hernial defect is demonstrable on one side, it can be presumed to exist on the opposite side in approximately 3 out of 4 cases.

CONCLUSIONS

1. Bilateral indirect inguinal hernia was found in 37 of 50 infants and children in whom only a one-sided hernia could be demonstrated preoperatively.

2. One hundred per cent of infants under 1 year of age had bilateral hernia whereas 65.8 per cent of children over 1 year of age were found to have hernias on both sides.

3. A bilateral surgical exploration seemed to be justified as it resulted in the cure of 37 undiagnosed indirect inguinal hernias.

4. The performance of a bilateral procedure obviates the necessity of a second hospitalization, second anesthesia, and second operative procedure.

5. The bilateral procedure does not add to length of hospital stay or operative morbidity.

6. There were no wound infections or operative complications in this series of cases.

REFERENCES

1. Potts, W. J., Riker, W. L., and Lewis, J. E.: The Treatment of Inguinal Hernia in Infants and Children, Ann. Surg. **132**: 566, 1950.
2. Iason, A. H.: Hernia, Philadelphia, 1941, The Blakiston Company, p. 169.
3. Gross, R. E.: Surgery of Infancy and Childhood, Philadelphia, 1953, W. B. Saunders Company p. 462.
4. Dunavant, W. D., and Wilson, H.: Inguinal Hernias in Infants and Children, J. Pediat. **44**: 558, 1954.
5. Zimmerman, L. M., and Anson, B. J.: Anatomy and Surgery of Hernia, Baltimore, 1953, Williams & Wilkins Co., p. 150.

Case Reports

RENAL ARTERIOVENOUS FISTULA

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MASS ligation of the renal vessels in nephrectomy, although almost uniformly practiced, is condemned by many surgeons as favoring the development of arteriovenous fistula. That this concern is unwarranted is revealed by the fact that a search of the literature fails to reveal a previous authenticated case of this complication.

Hollingsworth[1] reported a case following nephroureterectomy for renal tuberculosis. In this instance the renal vessels had been ligated separately but may have been traumatized by the aneurysm needle used to pass the ligatures. A bruit and thrill developed in the left flank eighteen months following the operation. There was progressive cardiac enlargement. The patient refused surgery, and when last seen, four years later, the bruit and thrill had diminished.

There are four other reported cases of renal arteriovenous fistula, none of which, however, was of apparent traumatic etiology. The first case reported was by Varela[2] in 1923 in a 28-year-old man with severe cardiac decompensation, mild hypertension, and a murmur in the right flank. At autopsy, a renal arteriovenous fistula was found, the etiology of which was presumed to be a congenital aneurysm of the renal artery with secondary erosion into the vein.

Rieder[3] reported a similar case in which a cure was effected by nephrectomy. His patient, preoperatively, had severe cardiac decompensation and hypertension, with a blood pressure reading of 220/110. A bruit was present in the right lumbar region. There was a history of right flank trauma, which may or may not have had any etiological significance. An aneurysm of the renal artery with erosion into the vein was revealed at the time of surgery.

Hamilton, Getz, and Jerome[4] reported a case in a renal carcinoma. The hypertension and bruit disappeared following nephrectomy. One additional case, which is not described, is mentioned in a personal communication from F. B. Camp to Lasher and Glenn.[5]

CASE REPORT

A 27-year-old white woman was admitted to Walter Reed Army Hospital on Feb. 6, 1954, with a chief complaint of exertional dyspnea and a constant severe left lower quadrant pain. In 1949 she had had a right nephrectomy for pyonephrosis complicating pregnancy. Two years later she developed her present complaints, which had persisted almost

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continuously since that time. Because of this pain she had two exploratory operations; one in 1951, when a bilateral salpingectomy was performed, and another in 1952, when an ovarian cyst was removed. In April, 1953, a diagnosis of endometriosis was made and she was castrated with x-ray. None of these procedures relieved her symptoms. Between April, 1953, and the present admission she had been hospitalized four times with severe left lower abdominal pain, vomiting, and distention. On none of these admissions was a cause for her complaints discovered, and she was given a diagnosis of psychoneurosis with conversion hysteria.

On admission to Walter Reed Army Hospital, examination revealed moderate non-radiating left lower abdominal tenderness but no palpable abdominal masses. Over the right lumbar region a definite thrill was palpated. On auscultation a harsh, machinery-like murmur was heard over the right flank scar with greatest intensity a handsbreadth to the right of the second lumbar vertebra. There was systolic accentuation of this murmur with no transmission. Compression of the flank failed to obliterate the thrill.

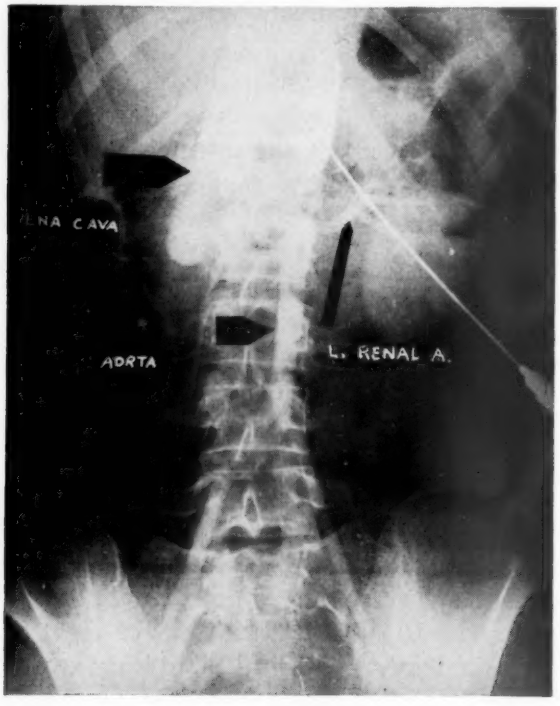

Fig. 1.

The heart was not enlarged. There was a Grade II systolic murmur heard over the precordium, which was not transmitted. The electrocardiogram was normal. The blood pressure reading in the upper extremities was 118/70. The blood pressure of the lower extremities was not recorded. The eye grounds were normal.

The gastrointestinal x-ray series, barium enema, blood chemistry, serology, hemogram, and urinalyses were not remarkable. An excretory urogram revealed an absent right kidney and an entirely normal left kidney.

Aortograms were obtained on three occasions before satisfactory visualization of the pathology was determined. This showed a normal left renal artery and kidney (Fig. 1). On the right, at the level of the right renal artery, there was a 2 cm. collection of the contrast medium with passage into and outlining the inferior vena cava. These findings

were consistent with a diagnosis of right renal arteriovenous fistula. For twenty-four hours following each aortogram the patient had excruciating left flank and left lower quadrant pain.

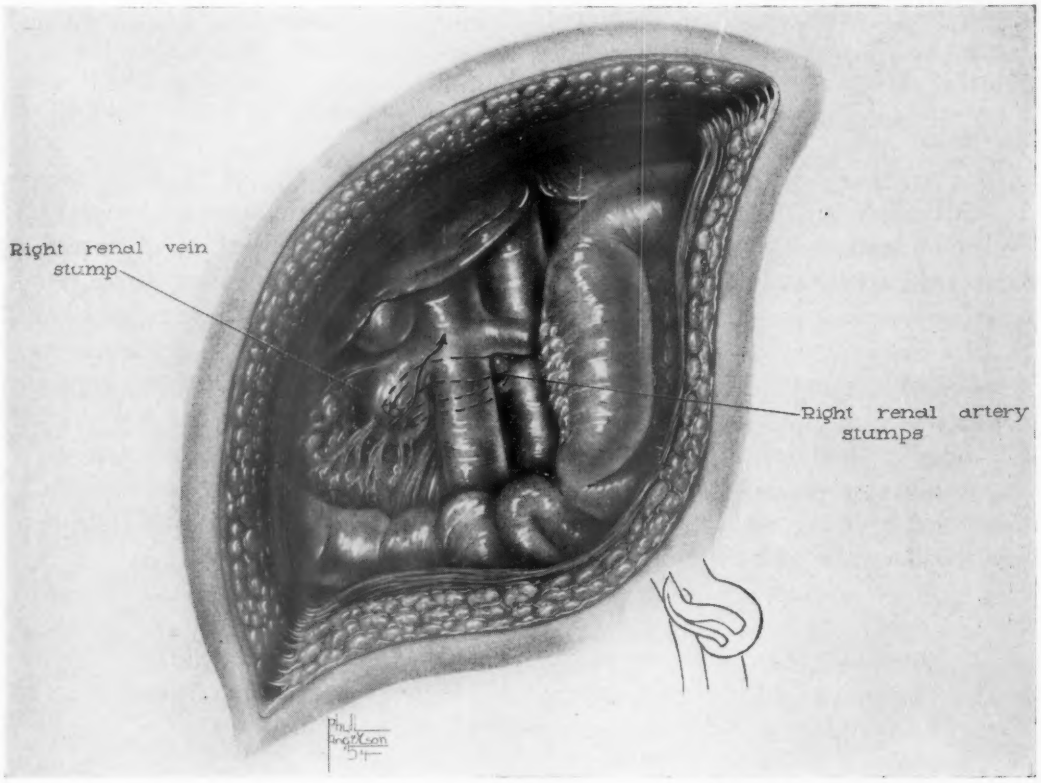

Fig. 2.

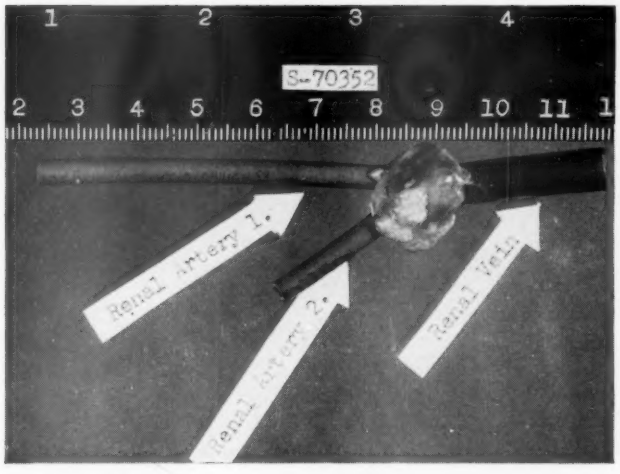

Fig. 3.

On March 9, 1954, the right renal arteriovenous fistula was excised through a right subcostal transperitoneal approach. The findings are diagrammatically presented in Fig. 2. A spherical pulsating mass about the size of a plum was discovered in the region of the

right renal vascular stump. The renal vein was first isolated, ligated, and divided. Two renal arteries were discovered entering the sac and were individually ligated and divided and the sac removed (Fig. 3). There was a 20 mm. narrowing of the pulse pressure when the vessels were clamped.

The patient's postoperative course was entirely uneventful. She experienced immediate and complete relief of the left lower quadrant pain and volunteered the information that for the first time in years she could breathe easier. The thrill and bruit were absent after the operation. She was discharged from the hospital on March 20, 1954.

COMMENTS

Although individual ligation of the renal vessels during nephrectomy is desirable from a technical standpoint, mass ligation as a cause of vascular complication is greatly exaggerated. In the extremely rare instance, where renal arteriovenous fistula complicates nephrectomy, the fistula is believed due to one of two causes: either the vessels retract within their ligated sheaths, or the vessels are traumatized proximal to their ligation by fixation sutures where those are used.

Lumbar aortography with demonstration of the dye in the vena cava is diagnostic of a vascular shunt. The treatment is surgical, and when the condition occurs on the right side, the transperitoneal approach, with mobilization and medial retraction of the duodenum, gives the best exposure.

SUMMARY

A case of renal arteriovenous fistula complicating nephrectomy for pyonephrosis and successfully treated by surgery has been presented. The role of lumbar aortography in diagnosis has been mentioned.

REFERENCES

1. Hollingsworth, K. W.: Arteriovenous Fistula of the Renal Vessels, Am. J. M. Sc. **188**: 399-403, 1934.
2. Varela, M. E.: Aneurisma arteriovenoso de los vasos renales y asistolia consecutive, Rev. méd. latino-am. **14**: 3244-3266, 1923.
3. Rieder, W.: Sonderstellung arterio-venöser Aneurysmen der Nierengefässe in Rahmen operativer Behandlung schwerer Herz-Krieslaufschäden beim arterio-venösen Aneurysma, Chirurg **14**: 609-618, 1942.
4. Hamilton, G. R., Getz, R. J., and Jerome, S.: Arteriovenous Fistula of the Renal Vessels: Case Report and Review of the Literature, J. Urol. **69**: 203-207, 1953.
5. Lasher, E. P., Jr., and Glenn, F.: Effects on Kidney and Blood Pressure of Artificial Communication Between Renal Artery and Vein, Arch. Surg. **38**: 886-905, 1939.

TUMOR OF THE VAGUS NERVE

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TUMORS of the vagus nerve are sufficiently rare to be worth while reporting. Neoplasms of this type are usually benign and well-encapsulated, there having been but two instances in the thirteen cases reviewed that were malignant.[6, 9] They arise from the sheath of the nerve and are referred to as schwannomas, neurilemmas, or neurinomas, as distinguished from tumors arising from the ganglia of the cranial nerve.[11, 15]

Symptoms are few and variable. Occasionally, symptoms of irritation of the vagus nerve, such as coughing, hoarseness, or tachycardia may be present. However, these are inconstant and not suitable for diagnostic purposes. The symptoms of chronic irritation of the vagus nerve are more prevalent if the tumor is malignant with invasion and/or destruction of the nerve fibers. In all of the cases cited previously, the sign which called attention to the tumor was a lump, or swelling, in the neck. In the intrathoracic vagus nerve tumors, a shadow on the chest roentgenogram was the outstanding sign. This was also true in the case cited here. Since localizing symptoms are not prominent, the diagnosis is usually made at the time of operation.[1] Any mass in the neck should be operated on and removed.

If the gross appearance is that of a benign, encapsulated tumor, an attempt should be made to remove the tumor mass without sacrificing the nerve itself. Some tumors may be dissected free of the nerve fibers. Occasionally, the nerve must be resected and an anastomosis of the vagus attempted. Dividing one vagus nerve in the neck may produce transient tachycardia,[8] aphonia, and difficulty in deglutition. Paralysis of the innervated vocal cord is a permanent complication.

CASE REPORT

Mrs. A. J., aged 51, was admitted to Mount Sinai Hospital on May 28, 1951, with the chief complaint of a swelling on the right side of the neck of two years' duration. Her past history included two previous Mount Sinai admissions, one in 1947 for a cholecystectomy for cholelithiasis, and one in 1948 for a postcholecystectomy syndrome. The present illness started with a right neck swelling which gradually grew larger. Nine months prior to admission, the patient began noting a sensation of pressure in the neck with choking, coughing when she bent forward, and moderate occasional difficulty in breathing. The patient had no symptoms of hyperthyroidism and still had mild symptoms of a postcholecystectomy syndrome.

Physical examination revealed blood pressure 150/70, pulse 60, respiration 16. Positive findings were a healed upper right rectus scar, a liver enlarged one fingerbreadth below the right costal border. In the neck on the right side was a mass, the size of a plum, smooth, soft, nonnodular, with no bruit or thrill. The mass was not fixed to the cervical

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structures. There were no palpable cervical lymph nodes. Preoperative examination of the vocal cords showed both moved well. Laboratory data were essentially normal, hemoglobin 13 Gm., basal metabolism rate minus 13.

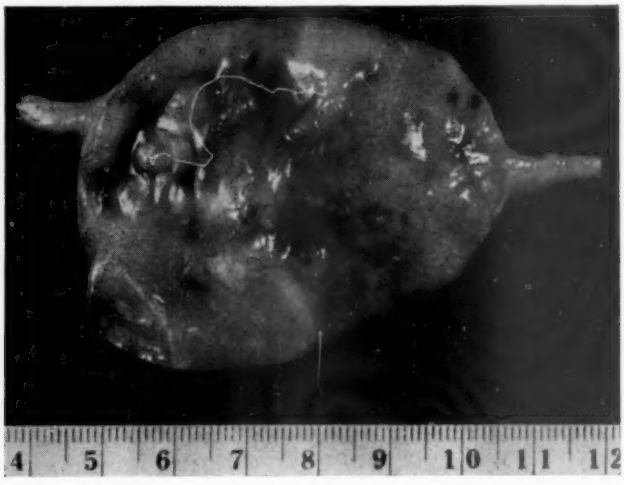

Fig. 1.—Photograph of excised tumor. Note the ends of the resected vagus nerve.

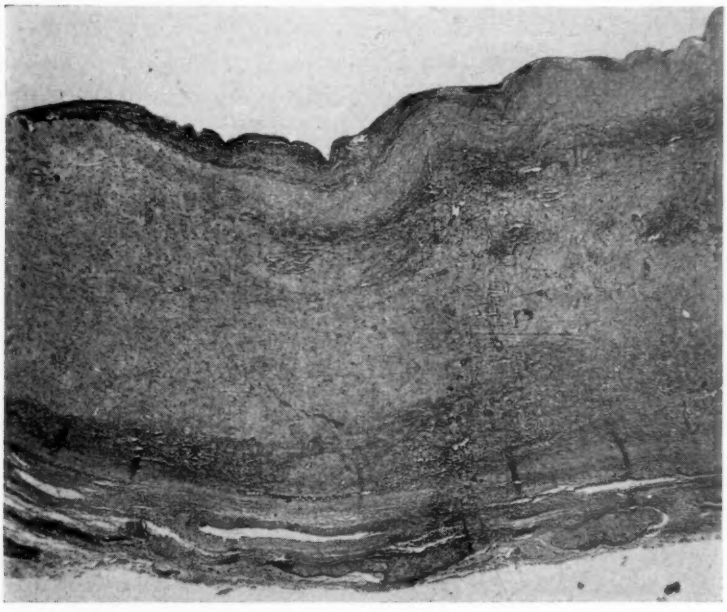

Fig. 2.—Low-power (×35; reduced ⅙) view of wall of tumor.

Course.—The patient was then prepared for surgery. Under general anesthesia, the neck was explored through a transverse incision. The mass, beneath the strap muscles, was found to be cystic, and entirely separate from the thyroid gland. It seemed to originate from the right vagus nerve, which was seen to enter the mass and then leave it. The nerve proper could not be dissected free of the tumor mass. Therefore, the nerve was divided above and below, and the neoplasm removed en bloc.

Postoperatively, the patient did well and was discharged to a convalescent home five days after the operation. Examination of the larynx postoperatively revealed absence of motion of

the right true vocal cord, the left cord moving well with an adequate airway. Three weeks later, the patient was readmitted for a suspected pulmonary infarction. She was discharged free of complaint two weeks later. She was last seen on June 25, 1954, with no evidence of recurrence and no complaints, except for slight residual hoarseness.

Pathology.—The specimen consisted of an elliptical cystic mass measuring 7 cm. in length and 4 cm. in circumference. At each pole of the mass is a 1 cm. long segment of nerve tissue. A section of the mass revealed a central area of cystic degeneration filled with hemorrhagic fluid, the solid portion of the neoplasm consisting grossly of grayish red fibrous tissue. The microscopic diagnosis was neurinoma with cystic degeneration (Figs. 1 to 3).

Fig. 3.—High-power (×250; reduced ¼) view of tumor. Illustrates the palisading of the nuclei.

COMMENT

Clinically, the cervical mass in the patient could not be differentiated from thyroid adenoma. At the time of operation, an attempt was made to dissect the tumor mass free and keep the vagus nerve intact. This was not feasible because the fibers became a part of the sheath of the tumor mass. The hiatus in the nerve was too great to attempt an anastomosis. Resection of the nerve did not seem to affect cardiorespiratory physiology of the patient, and paralysis of the right vocal cord was the only objective finding.

SUMMARY

A neurinoma in the cervical portion of the vagus nerve in a 51-year-old female is presented. The only symptom was a painless lump in the neck. Preoperative diagnosis was adenoma of the thyroid. Although benign, this tumor was excised together with the vagus nerve. Enucleation was attempted, but it could not be done. The only result of the severance of the vagus nerve was a unilateral recurrent nerve paralysis with moderate hoarseness of voice.

REFERENCES

1. Blades, B., and Dugan, D. J.: Resection of the Left Vagus Nerve for Multiple Intrathoracic Neurofibromas, J. A. M. A. **123**: 409, 1943.
2. Bruckschwiger, O.: A Case of Neurofibroma of the Vagus Nerve and the Symptoms of Vagus Irritation in the Clinical Diagnosis, Wein. klin. Wchnschr. **97**: 9, 1947.
3. Butos, F. M.: Schwannoma de Neumgiastico, Bol. y trab., Acad. argent. de cir. **29**: 448, 1945.
4. Cutler, E. G., and Gross, R.: Neurofibroma and Neurofibrosarcoma of Peripheral Nerves, Arch. Surg. **33**: 733, 1936.
5. Erlich, H. E., and Martin, H.: Schwannomas in the Neck and Head, Surg., Gynec. & Obst. **76**: 577, 1943.
6. Furber, E. D., and Fox, I. R.: Fibrosarcoma of the Left Vagus Sheath, West. J. Surg. **48**: 584, 1940.
7. Gerbode, F., and Marguiles, G. S.: Neurofibromatosis With Intrathoracic Neurofibromas of the Vagus Nerve, J. Thoracic Surg. **25**: 429, 1953.
8. Murley, R. S.: A Case of Neurinoma of the Vagus Nerve in the Neck, Brit. J. Surg. **36**: 107, July, 1948.
9. Parrella, G. S.: Neurofibrosarcoma of the Vagus Nerve, New England J. Med. **242**: 324, 1950.
10. Paul, M.: Nerve Sheath Tumors of the Vagus Nerve in the Neck, Australian & New Zealand J. Surg. **19**: 34 (Aug.) 1949.
11. Pirner, F. A.: A Ganglioneurinoma of the Vagus Nerve in the Neck, Zentralbl. Chir. **75**: 98, 1950.
12. Rosello, G.: Neurinoma of Vagus Nerve in the Left Latero-Gravico Site, Gior. ital. chir. **6**: 308, 1950.
13. Sekiguchi, S., and Oije, T.: Report of a Vagus Nerve Tumor, Arch. klin. Chir. **143**: 113, 1926.
14. Siebner, M.: Tumor of the Vagus Nerve in Presence of Generalized Neurofibromatosis, Deutsche Ztschr. Chir. **237**: 63, 1932.
15. Stout, A. P.: Specific Nerve Sheath Tumors (Neurilimoma), Am. J. Cancer **24**: 751, 1935.

GAS CYSTS OF THE INTESTINE

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THE clinical entity known as pneumatosis coli or pneumatosis intestinalis has a far more descriptive name—gas cysts of the intestine. This condition has been rarely described and rarely encountered, and its incidental discovery at the operating room table has usually been a source of surprise and consternation to the surgeon. Briefly, the condition is an accumulation of small to large cystlike structures in continuity with the gastrointestinal tract, and these cystlike structures may lie in the subserosal space or they may lie in the submucosal area. If they are lying in the subserosal space they are readily seen upon opening the abdomen and they can be best likened to a cluster of grapes of variable size, varying from 1 mm. in diameter to 5 to 10 cm. in diameter. If a cyst is ruptured there is an audible escape of gas which is odorless and which has been proved to be sterile under culture. If the submucosal area alone is involved the condition may not be recognized, although obstructive phases and distortion of the intestinal tract may suggest the site of pathology. The occurrence of air cysts along the intestinal tract was recognized by veterinarians for many years. The condition usually occurs in swine. It was first described in 1876 by Bang,[1] but the original American report was by Finney[2] in 1908. Turnure[3] added the second American case in 1913. These early cases were surgically explored for gastric pathology, and the finding of the gas cysts was incidental. The most exhaustive report was submitted by Jackson,[4] who accumulated 171 cases from the literature and added one of his own.

ETIOLOGY

The exact cause for the formation of the subserosal or submucosal gas cysts is unknown. Various theories have been expounded. Masson[5] thought that the gas cysts were dilated lymphatics, and he believed that the gas was produced by chemical action on the intestinal chyle. Naeslund and Berglund[6] thought that the gas was due to a coliform-like bacillus which penetrated the intestinal wall and produced the gas during growth. LaMont[7] believed that the gas formation was due to chemical reaction related to the absorption of the contents of a dilated bowel or stomach. These theoretical causes emphasize the neoplastic and the bacterial aspects, and are not as tenable as either the nutritional or the mechanical theory. The nutritional theory was given stimulus by Eveleth[8] in 1938. He was able to create this disease in hogs by restricting them to a rice diet. If corn was added to the rice diet the condition did not occur. The mechanical theory has gained popularity because with increased

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clinical experience there is associated gastrointestinal ulceration in a high percentage of cases. Turnure stated that 80 per cent of cases of pneumatosis intestinalis has associated severe gastrointestinal disease. Lindsay and associates[9] reported 45 per cent had associated duodenal ulcer. They raise the question as to the part played by hyperperistalsis. The mechanical theory presupposes a mucosal break and the propulsion of gases along the submucosal or subserosal plane.

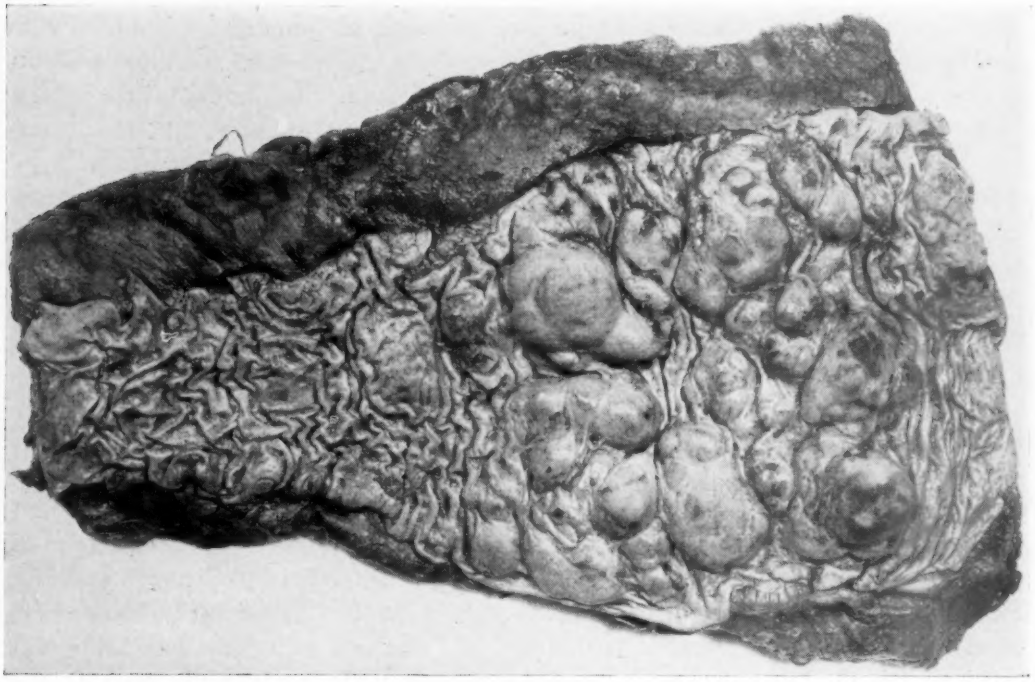

Fig. 1.—Sigmoid colon with what appears to be a polypoid lesion. Perforation of the individual cysts results in a collapse of the mucous membrane to its normal state.

PATHOLOGY

On gross examination this condition is characterized by collections of gas under the serosa or mucosa most frequently in relationship to the terminal ileum. The individual cyst may vary greatly in size and has been seen in the distal ileum, the cecum, the ascending colon, the jejunum, the omentum, and also along the gastrohepatic ligament. Masson stated that gas cysts never occur along the descending colon, but we have a case to disprove this point. If the gas cysts are in the subserosal layer they may cause angulation of the intestine. They are most frequently seen on the antimesenteric border, where they appear as clear translucent bubbles. The submucosal variety, of course, cannot be directly visualized until the intestinal tract has been opened, and when this has been done the multiple cysts give the mucosa a pebbled appearance. If the large bowel is palpated one can gain the impression of malignant tumor growth. As has been stated previously, bacterial study of the gas cyst has revealed nothing. Microscopic study of the cysts shows a rather extensive chronic

cellulitis in which granulation tissues are formed that have variable numbers of foreign-body giant cells. In addition, there is a formation of cystlike structures, some of which seem to have a flattened epithelial lining, but others are lined by a layer of foreign-body granulation tissue. The muscularis usually shows no significant inflammatory reaction.

Fig. 2.—Colon study with barium five years after the local resection. There has been no remission of the process. The gas cysts are seen most numerous in the splenic flexure.

SYMPTOMATOLOGY

There is no definite chain of symptoms which would lead one to suspect gas cysts. The symptomatology depends entirely upon their location, not only in relation to the entire intestinal tract but also in relation to the submucosal or subserosal regions. The diagnosis is usually made at the operating room table, although recently it has been shown that a preoperative diagnosis can be established.

DIAGNOSIS

This condition has occurred in both children and in adults. In Jackson's series of 172 cases, twelve cases occurred in children and 160 occurred in adults. In 1929 Moore[10] reported four cases in infants and stated that in the young patient the location of the cyst is usually submucosal, whereas in adults it is usually subserosal. Lerner and Gazin[11] were of the opinion that this entity can be diagnosed preoperatively by x-ray investigation. They felt that the

presence of inconstant filling defects of increased translucency is pathognomonic, and they reported a case of cecal pneumatosis in a 22-year-old man who recovered without surgical interference. Matranola[12] thought that the most important x-ray finding was the absence of intestinal loops between the diaphragm and the liver.

We would like to report a case of submucosal gas cysts of the left colon, in which one of us (G. V. P.) operated five years ago for an obstructive lesion of the left colon. This case is of clinical importance because the patient has been under constant observation for the past five years. Repeat x-ray examinations following surgery have shown that there has been an extension of this process proximally along the descending colon.

Mr. J. C. M., a 61-year-old white man, entered St. Luke's Hospital on Jan. 27, 1949. For a period of five months he had been complaining of alternating constipation and diarrhea, and his family physician had ordered a colon study. This barium study made at another hospital revealed a definite filling defect in the upper sigmoid colon, and his entry into St. Luke's Hospital was primarily for definitive surgical treatment. Following medical preparation he was taken to the operating room and the abdomen was explored through a left lower mid-rectus incision. The sigmoid colon was rather easily delivered, and palpation revealed a four-inch area of thickening in the upper one-half of the sigmoid colon. This area felt nodular, and it was our gross impression that it represented a polypoid carcinoma. Exploration of the abdomen was otherwise negative and the usual sigmoid resection was begun. Examination of the resected colon revealed a series of bubblelike structures (Fig. 1), which had a glassy translucent appearance and which, when penetrated with the sharp point of a scalpel, emitted a hissing tone due to the escape of gas under pressure. On decompression of these individual bubbles, the mucosal pattern appeared normal, and we could have continued penetrating these individual cysts until our entire pathology had disappeared under our eyes. Happily this patient recovered without incident and left the hospital on the tenth postoperative day. Since his surgery he has had colon studies each six months. He was placed on a high-vitamin diet and had supplemental B complex injections. Each x-ray study showed a progression of his "disease." There now appear to be multiple gas cysts from the point of resection well up into the splenic flexure (Fig. 2). At the present time he is asymptomatic and would be considered to be in excellent health.

We think this case is of interest because it has shown no tendency toward spontaneous remission. It was also of clinical value because the submucosal cysts created obstructive symptoms which led to surgical resection.

REFERENCES

1. Bang, B. L. F.: Luftholdige kyster i vaggen af ileum og i nydannet bindevav pa sammes serosa (Cysts in the Walls of Ileum and in Neoplasm of Connective and Serous Tissue), Nord. med. Ark. **8:** 18, 1876.
2. Finney, J. M. T.: Gas Cysts of Intestine, J. A. M. A. **51:** 1291, 1908.
3. Turnure, P.: Gas Cysts of Intestine, Ann. Surg. **57:** 811, 1913.
4. Jackson, J. A.: Gas Cysts of Intestine, Surg., Gynec. & Obst. **71:** 675, 1940.
5. Masson, P.: La lymphopneumitose cystique, Ann. anat. path. **2:** 541, 1925.
6. Naeslund, J., and Berglund, S. (1924), reported in Berglund, S.: Roentgen Diagnosis of Pneumatosis Cystoides Intestinalis, Acta radiol. **20:** 401, 1939.
7. LaMont, D.: Cystic Pneumatosis of Bowel, Royal Med. Chir. Soc. **23:** 113-118, 1928-1929.
8. Eveleth, D. F., and Beister, H. E.: Further Studies on Intestinal Emphysema of Swine, Am. J. Hyg. **27:** 364-369 (March) 1938.
9. Lindsay, J. W., Rice, E. C., and Selinger, M. A.: Pneumatosis Cystoides Intestinalis in Infants, Arch. Path. **30:** 1085, 1940.
10. Moore, R.: Intestinal Pneumatosis, Am. J. Dis. Child. **38:** 818, 1929.
11. Lerner, H. H., and Gazin, F. E.: Pneumatosis Intestinalis; Its Roentgenological Diagnosis, Am. J. Roentgenol. **56:** 464, 1946.
12. Matranola, cited by Lindsay.[9]

BILATERAL SPIGELIAN HERNIAS IN CHILDHOOD

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A SPIGELIAN hernia may be defined as a hernia through the linea semilunaris (Spigelius' line) in the anterior abdominal wall, along the outer border of the rectus sheath, at or below the level of the semilunar fold of Douglas. Such hernias are quite uncommon, and the reported cases to date have been almost completely confined to adults. A recent opportunity to treat a boy with bilateral Spigelian hernias has prompted this study, which apparently records the first description of such a situation in the pediatric age group.

CASE REPORT

A. O., Montefiore Hospital admission number 67538, was an 8-year-old white boy with asymptomatic bilateral oval protrusions in the anterolateral portions of the abdominal wall. The child had just recovered from moderately severe measles, and the previously unsuspected bulges had been noted in the course of a routine checkup examination by the pediatrician.* The abnormalities could be detected only when the child was straining. On examination he was a healthy-appearing, alert, normally developed child of stated age. A discrete oval bulge could be seen in the right lower quadrant, just lateral to the rectus muscle, slightly below the level of the anterior superior iliac spine (Fig. 1). There was an underlying oval musculofascial defect, measuring 2.5 cm. in its long axis, and transmitting an impulse on coughing. A similar, smaller bulge was located symmetrically in the comparable location in the left lower quadrant.

Re-examination after a four-month interval showed no change on either side, and the right Spigelian hernia was repaired surgically on June 14, 1954. A slightly oblique transverse incision was made through the skin and subcutaneous tissue in the right lower quadrant, directly over the hernia. The aponeurosis of the external oblique muscle was attenuated overlying the defect, and was incised in the line of the incision. An oval gap was present in the internal oblique muscle, directly over a sharply defined crescentic defect in the transversus muscle. This was immediately lateral to the semilunar line, and just below the fold of Douglas. There was no true sac, and the peritoneum was not opened. The fascial edges of the ring were approximated, and the defect in the internal oblique muscle was united. Because the attenuated external oblique aponeurosis seemed to offer little for reconstructive purposes, a generous flap of anterior rectus sheath was mobilized, and sutured over the entire defect. The external oblique was reunited, and the skin closed. Interrupted sutures of silk were used throughout the operation.

The child was discharged from the hospital on the day following operation, the sutures were removed one week later, and the wound healed by primary union. Re-examination four months later showed a firmly healed incision, with no evidence of recurrence (Fig. 2). The Spigelian hernia on the left has remained stationary in size, and this will remain under observation.

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*Dr. David Rosenberg.

A.

B.

Fig. 1.—*A* and *B*, Preoperative appearance of right Spigelian hernia.

A.

B.

Fig. 2.—*A* and *B*, Appearance four months postoperatively.

DISCUSSION

Spigelian hernias occur relatively infrequently. In 1919, Barthélemy[1] summarized the literature and found only twenty-two cases. In 1951, Mersheimer, Winfield, and Ruggiero[2] collected 157 reported cases, and added four of their own. Koontz,[3] in that same year, described seven cases before the Southern Surgical Association, three of which were proved at operation. Recently three additional cases were recorded by Zimmerman and Anson,[4] bringing the total to 171. The number of Spigelian hernias reported in the last several years has increased rapidly. This, with the experiences of Zimmerman and Anson in the anatomy laboratory, would suggest that the condition is not as uncommon as is implied by the literature.

Bilateral spontaneous Spigelian hernias are truly rare. River[5] found only three individual case reports, all in the foreign literature, prior to 1942. The cases all involved adults, and there have apparently been no previous reports of bilateral Spigelian hernias in children, as recorded in the *Quarterly Cumulative Index Medicus* for the past thirty years and in the standard references on the subject of hernias. The single paper describing unilateral Spigelian hernias in children includes three siblings all of whom died in the neonatal period with congenital strangulated hernias of this type.[6] Gross has been unable to recall a Spigelian hernia at the Children's Medical Center in Boston, and Kirklin stated that none have been encountered in children at the Mayo Clinic.[7]

The linea semilunaris or Spigelian line corresponds to the lateral margin of the rectus sheath, and runs from the ninth costal cartilage to the pubic spine. It is formed by the aponeurosis of the internal oblique muscle at its line of division to enclose the rectus muscle, and reinforced anteriorly by the aponeurosis of the external oblique and posteriorly by that of the transversus abdominis. Midway between the umbilicus and the symphysis pubis, down to the pubis, the posterior rectus sheath is absent, as the internal oblique fails to split into two leaves, but passes in front of the rectus muscle with the aponeurosis of the external oblique and transversus muscles. The lower border of the posterior sheath between the umbilicus and pubis forms a curved horizontal arch called the linea semicircularis or fold of Douglas. The inferior epigastric artery enters the rectus sheath by crossing this edge in the majority of cases. However, in less than 50 per cent of individuals the artery perforates the posterior sheath just above the linea semicircularis.

The term "Spigelian hernia" is reserved for those hernias which present along the semilunar line. A great majority of these appear at or below the fold of Douglas. There has been some confusion concerning the classification of those hernias emerging below the inferior epigastric artery in the semilunar line. Some authors have considered these as a variety of Spigelian hernia, while others have classified them as direct inguinal hernias. Recent authors have evaded attempts to differentiate between these entities in this location on the basis that the differentiation is of academic interest and without clinical application. Both Downes[8] and Mathews,[9] however, did attempt to distinguish between

hernias in this area by using the lateral umbilical ligament as a landmark. Semilunar hernias appear medial to the ligament, while direct inguinal hernias appear lateral to it. This is true in most instances, but is not infallible.

The etiology of these hernias has been poorly understood, and numerous theories have been advanced to account for this condition. Sir Astley Cooper, in 1804, first suggested that these hernias presented through vascular foramina. Numerous authors supported this thesis and implicated the hiatus around the inferior epigastric artery as it perforates the posterior sheath. Others[10] considered this condition to be due to a weakness of the abdominal wall at the junction of the semilunar line and semicircular fold of Douglas. There the posterior sheath abruptly ends, and there is no aponeurotic support between the transversalis fascia and the musculature of the abdominal wall. Recently Zimmerman, Anson, Morgan, and McVay[11] undertook in the anatomy laboratory to determine the aponeurotic and muscular arrangement of the abdominal wall. They dissected 500 body halves and found there was a wide variation in the relative amounts of muscular and aponeurotic tissue in the transverse and internal oblique muscle layers. Contrary to the popular impression, these muscles are not always uniform throughout, but are often composed of divergent bundles of muscle fibers separated by slitlike gaps of aponeurotic tissue. The width of these defects varied from 0.2 cm. to 1.5 cm. In a series of 100 body halves they found such defects in one or both layers in forty-five specimens. Ten specimens had defects in both layers, and in six they were superimposed. It is their opinion that these hernias emerge through defects formed by the banding of the muscle fibers. In several instances they encountered actual hernias at the dissection table.

The concept of segmental banding of muscle bundles would seem more likely as an underlying basis for the formation of Spigelian hernias than any weakness of the linea semilunaris itself. On the contrary, the latter structure, representing a line of fusion of aponeurotic and muscular elements, represents an area of strength. For the most part, the segmenting of muscle groups was noted in the region of the semicircular junction. These muscular architectural defects are quite common, and it is necessary for other contributing factors to be present in order to produce a hernia. Increased intra-abdominal tension is the most prominent of these. Pregnancy, obesity, ascites, and chronic cough have been frequent findings in patients with these lesions. The possible relationship of measles to the hernias in the present case can only be speculative. It would seem far more likely that the muscular defects had been present for some time, rather than that a unique type of muscular degenerative process occurred in the course of or as the result of the measles.

These hernias are usually asymptomatic and, when irreducible, may be difficult to distinguish clinically from abdominal wall tumors. Interstitial hernias must also be considered in the differential diagnosis.

Effective treatment for this condition is always surgical. The operation consists of exposing the hernia by dividing the external oblique aponeurosis. A properitoneal ball of fat may be adherent to the sac, and when present these

must both be dissected from the surrounding tissue. The fat is resected and the sac ligated and divided at its neck, after reducing its contents. The hiatus in the muscular layers, which is usually well defined, is then closed and the external oblique reapproximated. In the present instance repair was accomplished by imbricating and reinforcing the muscular structures without the necessity for entering the peritoneal cavity. It is felt that mobilizing a flap of rectus sheath to serve as a buttress over the defect may add to the repair. As long as the protrusion at the left Spigelian site on straining remains small and asymptomatic, there would seem to be no compelling indication for surgical correction. The future of this lesion will be of considerable interest.

SUMMARY

1. A case report of bilateral Spigelian hernias in a child has been presented. This apparently represents the first recorded instance of this condition in a child.

2. The anatomy, etiology, diagnosis, and treatment of this entity are discussed.

REFERENCES

1. Barthélemy, M.: Les hernias abdominales latérales, Bull. et. mém. Soc. chir. Paris **45:** 1313, 1919.
2. Mersheimer, W. L., Winfield, J. M., and Ruggiero, W. F.: Spontaneous Lateral Ventral Hernia. So-called Spigelian Hernia, Arch. Surg. **63:** 39, 1951.
3. Koontz, A. R.: Hernia in the Linea Semilunaris, Ann. Surg. **135:** 875, 1952.
4. Zimmerman, L. M., and Anson, B. J.: Anatomy and Surgery of Hernia, Baltimore, 1953, Williams & Wilkins Company.
5. River, L. P.: Spigelian Hernia, Ann. Surg. **116:** 405, 1942.
6. Scopinaro A. J.: Hernia on Spigels' Semilunar Line in a Newborn, Semana méd. **1:** 284, 1935.
7. Gross, R. E., and Kirklin, J. W.: Personal communications.
8. Downes, W. A.: Management of Direct Inguinal Hernia, Arch. Surg. **1:** 53, 1920.
9. Mathews, F. S.: Hernia Through the Conjoined Tendon, or Hernia of the Linea Semilunaris, Ann. Surg. **78:** 300, 1923.
10. Watson, L. F.: Hernia, ed. 3, St. Louis, 1948, The C. V. Mosby Company.
11. Zimmerman, L. M., Anson, B. J., Morgan, E. H., and McVay, C. B.: Ventral Hernia Due to Normal Banding of the Abdominal Muscles, Surg., Gynec. & Obst. **78:** 535, 1944.

RUPTURE OF THE STOMACH IN THE NEWBORN INFANT WITH SURVIVAL

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RUPTURE of the stomach in the newborn infant is a rare entity, especially when due to a congenital defect of the musculature, but may be more common than reported. Twenty-nine cases have been reported to date[1-11]; this case we believe to be the thirtieth and representing the fifth survival. Leger, Ricard, Leonard, and Piette[5] reported the first survival in 1950. Ross, Hill, and Haas,[7] Braunstein,[9] and Northway, DeLano, and Claytor[10] have also reported survivals. This condition is more commonly found in males. The patients which survived surgery had perforations along the greater curvature, varying from 2 cm. upward. There were no associated intestinal anomalies in the surviving cases, and no biopsies were taken at the time of surgery.

Perforation of the stomach falls into four main categories[9]: secondary to (1) ulcer, (2) injury due to gavage, (3) congestion due to septicemia and asphyxia, and (4) defects in the musculature of the gastric wall. Our case falls into the fourth category. Griffin and Griffin[11] surveyed the literature and found only four cases in which a rent in the stomach wall was caused by a defect in the musculature. Since then, Braunstein[9] reported five additional cases and the tenth case was reported by Northway, DeLano, and Claytor.[10] We believe our case to be the eleventh reported in this category.

CASE REPORT

D. E., a Negro male infant, weighing 7 pounds, 15½ ounces was born at Mount Sinai Hospital on Sept. 6, 1954, at 3:42 P.M., after a normal pregnancy and spontaneous uncomplicated delivery. He was a product of forty weeks' gestation and cried spontaneously. The mother was a 23-year-old Negro primipara with a past history of asthma in childhood. Her general physical examination was within normal limits, including the pelvic measurements. She was Rh positive and had negative serology. Normal labor was thirteen hours, forty-four minutes in duration—first stage thirteen hours, twenty-five minutes, second stage seventeen minutes, and third stage two minutes.

Initial physical examination revealed the infant to be in good health without any obvious congenital anomalies. He was admitted to the nursery at 5:05 P.M. and was subsequently re-examined and found to be in good condition with no abnormalities. Temperature was 97° F. A heat lamp was applied. At 1:00 A.M. on Sept. 7, 1954, the infant passed a large meconium stool. At 6 A.M. he was given 0.5 ounce of water, which was retained. At 8 A.M. he had a small yellow stool. At 10 A.M. the patient went to the breast and also took 0.25 ounce of tea. At 4 P.M. a large green stool was passed. At 6 P.M. he had a breast feeding and 0.5 ounce of tea. At 8 P.M. a small green stool was passed. At 10 P.M. the baby had a breast feeding and 1 ounce of tea. On Sept. 8, 1954, at 1:00 A.M. the patient passed a large green stool. At 2 A.M. 1.25 ounces of formula (evaporated milk and water) was given and regurgitated. At 6 A.M. he retained a breast feeding and 1 ounce of tea. At 8 A.M. a

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small meconium stool was passed. At 10 A.M. he refused to nurse at the breast. The abdomen became firm and distended. At 11 A.M. the patient refused formula. At 12 noon a tap-water enema was given with the clear water being returned. The distention was unchanged. At 1 P.M. the abdomen was still distended, tympanitic, and nontender; liver dullness was obliterated. The infant was somewhat dehydrated and listless. The chest was hyperresonant to percussion, but breath sounds were normal. The anterior fontanel was not distended. Rectal examination with the little finger revealed no obstruction and exceedingly free mobility of the colon. It could be moved in all directions without meeting resistance, giving the impression that it was suspended in space. Sickle-cell test was negative.

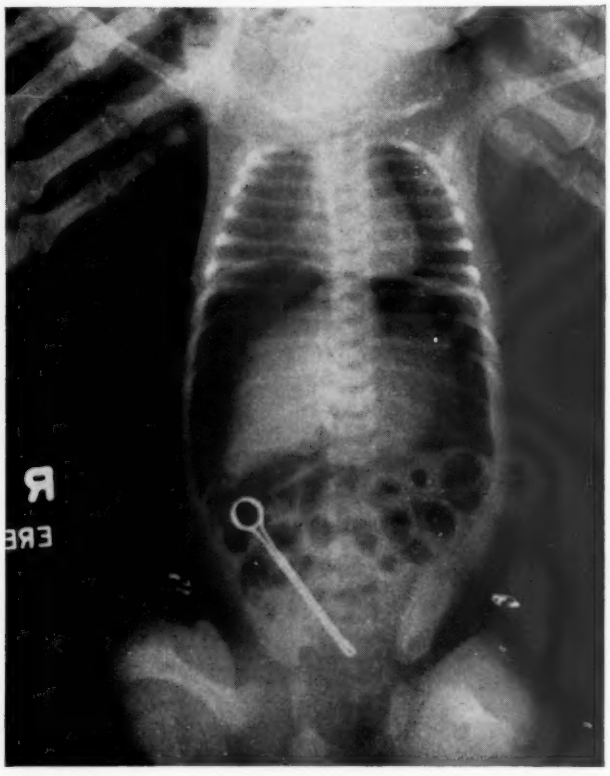

Fig. 1.—Roentgenogram in the upright position showing pneumoperitoneum and absence of air bubble in the stomach. Gas is present in the small and large bowels.

Roentgenograms were taken (upright and recumbent views) revealing pneumoperitoneum (Figs. 1 and 2). The liver and spleen were pushed down, and free air was present under the diaphragm. There was no gas bubble present in the stomach, but gas was present in the large and small bowel, as in the case reported by Ross, Hill, and Haas.[7] Therefore, a diagnosis of a ruptured stomach was made and immediate surgery advised.

Ten hours following the onset of distention, with drop ether anesthesia, the abdomen was opened through a right paramedian incision. As the peritoneum was opened, air escaped under pressure, making a noise similar to that of air escaping from a tire. There was bile-stained fluid present in the abdomen. The entire greater curvature of the stomach (about 2.5 inches in length) was ruptured. There was no bleeding from the edges of the area of the stomach rupture and no reaction indicative of a peptic ulcer. The closure was in layers, the first being continuous catgut and the second interrupted silk. A third layer of interrupted silk was placed where it was felt the suture line was weak. Thorough exploration was carried out and no other perforations or congenital anomalies were present. As much of the fluid as possible was removed by suction from the peritoneal cavity. Practically no milk was present in the peritoneal fluid. The closure of the abdomen was in layers.

The catheter which had been inserted through the nose into the stomach preoperatively was allowed to remain in place. The infant was given about 80 c.c. of blood postoperatively (10 c.c. per pound of body weight) and supported with parenteral fluids to which were added 50 mg. of vitamin C and 10 mg. of vitamin K daily. Penicillin, 100,000 units, and dihydrostreptomycin, 0.125 Gm., were given twice daily for five days. Bowel sounds were heard on the second postoperative day and so the tube was clamped at intervals. On the third postoperative day 5 c.c. of 5 per cent glucose solution in water was given hourly through the catheter.

Fig. 2.—Roentgenogram taken in recumbent position.

The tube was removed on the fourth postoperative day and 5 c.c. of 5 per cent glucose solution and 5 c.c. of breast milk were given hourly. On the fifth postoperative day the infant was placed on a regular pyloric regime, being given 15 c.c. of water and 15 c.c. of breast milk hourly, gradually increasing the quantity until the child was receiving normal feedings every eight hours. The abdominal wound healed per primum. He was discharged from the hospital on Sept. 17, 1954. He was last examined on Nov. 1, 1954, weighing 10 pounds, 6 ounces and found to be in excellent health.*

DISCUSSION

X-ray examination in the erect and recumbent positions should be carried out in all cases of distention in the newborn infant because early diagnosis of a perforated viscus and early operation give a better chance of survival. We do not recommend that barium or Lipiodol should be given in these cases in that sufficient information can be obtained without their use and, second, we feel that these agents in the peritoneal cavity further add to the peritonitis and possibly impair healing of neonatal tissue.

*The patient was seen in consultation by Dr. J. Aranow, associate attending pediatrician.

This case falls into the category of being secondary to a congenital defect in the musculature. At the time of surgery, we did not find evidence of peptic ulceration nor any bleeding from the walls of the ruptured portion of the stomach. We agree with Griffin and Griffin[11] in that we believe a high percentage of the reported gastric ulcers in the newborn infant are on the basis of a muscular defect and not on an ulcer basis. The surgeon at the operating table cannot accurately differentiate between the two conditions and, second, most of these ruptures occur at the greater curvature, where peptic ulceration is known to be uncommon. There was practically no milk in the abdominal cavity at the time of surgery, indicating that the food passed along the magenstrasse. No biopsy was taken at operation because it was felt that the best procedure was to close the defect in the stomach as rapidly as possible, performing only the necessary surgery.

In none of the reported surviving cases was biopsy taken. Complete exploration is necessary at the time of operation to find all defects.

SUMMARY

A case of rupture of the stomach in the newborn infant, secondary to a congenital defect in the musculature, occurring forty-five hours after birth is presented. We believe this to be the fifth case reported in the literature which has survived. Prompt diagnosis and early operation to correct this defect are believed to be the main factors for survival. A distended abdomen, absent bowel sounds, and free mobility of the large bowel on rectal examination are presumptive findings of a ruptured viscus which can be corroborated by x-ray examination in the upright position. The presence of a pneumoperitoneum with air in the small and large bowels and the absence of an air bubble in the stomach should be diagnostic of a ruptured stomach.

We wish to commend the nurses for the splendid care this child received and the cooperating departments of Mount Sinai Hospital.

REFERENCES

1. Herbut, P. A.: Congenital Defect in the Musculature of Stomach With Rupture in Newborn Infant, Arch. Path. **36:** 91-94 (July) 1943.
2. Rosenberg, A. A., and Heath, M. H.: Acute Gastric Ulcer With Perforation in One of Premature Twins, J. Pediat. **28:** 93-95 (Jan.) 1946.
3. Pendergass, E. P., and Booth, R. E.: Report of Case of Ruptured Stomach in an Infant Three Days Old, Am. J. Roentgenol. **56:** 590-593 (Nov.) 1946.
4. Burnett, H. A., and Halpert, B.: Perforation of the Stomach of a Newborn Infant With Pyloric Atresia, Arch. Path. **44:** 318-320 (Sept.) 1947.
5. Leger, J. L., Ricard, P. M., Leonard, C., and Piette, J.: Ulcère gastrique perforé chez un nouveau-né avec survie, Union méd. Canad. **79:** 1277-1280 (Nov.) 1950.
6. Wright, L. T., and Scott, B. E.: Perforated Gastric Ulcer in a Newborn Infant, J. Pediat. **37:** 905-908 (Dec.) 1950.
7. Ross, M., Hill, P. S., and Haas, C. M.: Neonatal Rupture of the Stomach, J. A. M. A. **146:** 1313-1314 (Aug.) 1951.
8. Greene, W. W., and Gose, D. F.: Perforation of the Stomach in the Newborn, Am. J. Dis. Child. **85:** 47-51 (Jan.) 1953.
9. Braunstein, H.: Congenital Defect of the Gastric Musculature With Spontaneous Perforation, J. Pediat. **44:** 55-63 (Jan.) 1954.
10. Northway, R. O., DeLano, R. H., and Claytor, R. R.: Perforation of the Stomach in the Newborn Infant, SURGERY **35:** 925-927 (June) 1954.
11. Griffin, J. P., and Griffin, C. G.: Perforation of the Stomach in a Newborn Due to a Congenital Defect, J. Indiana M. A. **47:** 619-621 (June) 1954.

PRIMARY MALIGNANT MELANOMA OF THE FEMALE URETHRA

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THE case of primary malignant melanoma of the female urethra reported herein is of interest for three reasons: (1) this condition is comparatively rare, (2) the tumor apparently metastasized to the cervix and vaginal mucosa by local implantation, and (3) the patient is living without any indication of the disease over three years after excision of the primary lesion and over one year following excision of the metastatic foci.

The rarity of melanoma of the female urethra is evidenced by the fact that a rather thorough search of the literature by Long, Counseller, and Dockerty[1] in 1946 revealed only eleven cases previously reported. The three which they reported made a total of fourteen cases in the literature to that time. Savran, Sayer, and Schradiack,[2] in 1948, reported a case of a 70-year-old woman with a primary melanoma of the urethra which was treated by local excision. Their patient died nineteen months following the operation.

Allen and Spitz,[3] in a review of 934 melanomas from the Memorial Hospital in New York, mentioned one case in which the lesion was located at the urethral meatus. It was inferred, but not stated, that this was in a female. No details of the case were given except that the patient had died. The case herein reported presumably is the seventeenth thus far reported.

REPORT OF A CASE

Mrs. H., a 77-year-old white woman, was first seen on May 10, 1950, her chief complaint being recurrent nausea and vomiting for a period of one month. She had previously had no symptoms referable to the gastrointestinal tract, nor had she at any time experienced any difficulty referable to the genitourinary tract. The only other complaint was dyspnea on exertion, of several months' duration.

Physical examination and laboratory and roentgen studies failed to demonstrate any lesion of the gastrointestinal or genitourinary tract. It was found, however, that the patient had auricular fibrillation and calcification of the abdominal aorta, for which she was given medication.

In October, 1950, she returned to the clinic because of a small growth on the bridge of the nose, which had been present for six months. The lesion proved to be a basal-cell epithelioma and was successfully treated by roentgen therapy.

The patient was next observed in January, 1951. At that time she complained of a bright red vaginal spotting of one week's duration, and of loss of energy. Since her menopause 27 years previously, she had never noticed any vaginal bleeding prior to this occasion.

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On examination, a small, red, granular-appearing growth was discovered on the urethra. No other abnormality was found on physical or routine laboratory study. The growth was believed to be a caruncle and was excised in the office. The pathologist made a diagnosis of malignant melanoma.

A follow-up examination in November, 1951, revealed the site of the excision to be well healed.

On Jan. 23, 1952, the patient returned and reported having had a slight amount of bright red vaginal bleeding for the previous six weeks. At this time, a polypoid lesion approximately 1.5 cm. by 0.5 cm. in size was found at the urethral orifice. The tumor had a granular appearance and bled easily. It was excised with a wide margin of the surrounding normal tissue and, again, the pathologic diagnosis was malignant melanoma.

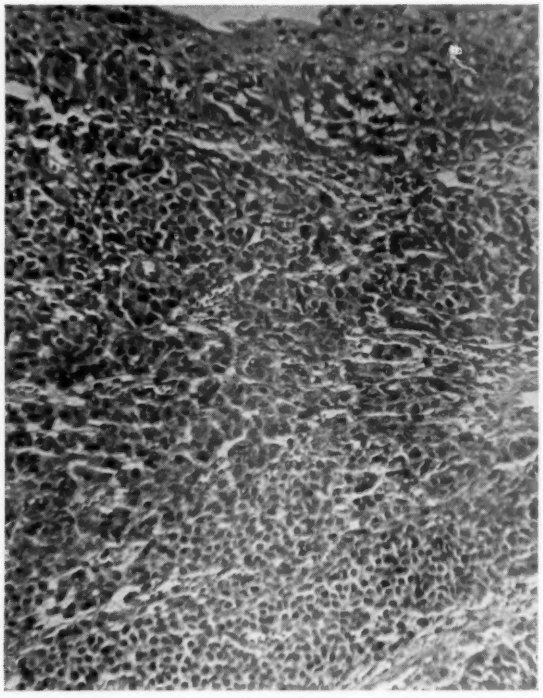

Fig. 1.—Primary urethral malignant melanoma (×100; reduced ¼).

At the patient's next visit, in June, 1952, the area of the excision was well healed and there was no evidence of recurrence. On the anterior lip of the cervix, however, was a small, dark, granular area which bled easily. This was believed of no significance and, unfortunately, was not investigated further. The same error was made on a subsequent visit of the patient in October, 1952; at that time the cervical lesion was present but unchanged.

The patient was not observed again until Aug. 10, 1953, when she returned because of a slight vaginal bleeding of one week's duration. Inspection revealed a dark-colored lesion approximately 1 cm. in diameter in the central portion of the cervix. The lesion bled slightly on contact. Another dark area, 1.5 cm. in diameter, was found on the mucous membrane of the vaginal introitus. There were no signs of a recurrence in the region of the urethra, and nothing new otherwise was found on general physical examination, on routine laboratory studies, or in a roentgen study of the chest. The report from a cytologic study of a vaginal smear indicated a need for further diagnostic investigation.

On Aug. 17, 1953, a total abdominal hysterectomy was performed, and the dark area at the vaginal introitus was excised. A thorough examination of the abdomen and viscera revealed no signs of metastases. There were no enlarged pelvic, iliac, or para-aortic lymph nodes. At the patient's most recent observation, on Aug. 3, 1954, one year after the hysterectomy, no metastatic or recurrent disease was found.

The pathologist reported that the original specimen submitted under a clinical diagnosis of urethral caruncle was an irregularly shaped portion of red-tan colored tissue with a granular, friable surface. Microscopic examination showed cords and nests of atypical polygonal cells with numerous mitotic figures (Fig. 1). Some of the cells contained brown pigment structurally consistent with melanin.

The specimen submitted in January, 1952, was similar both grossly and microscopically to the original specimen.

Fig. 2.—Uterus, showing area of metastatic melanoma in the cervix.

The ovaries, tubes, and body of the uterus examined following the panhysterectomy were essentially normal. The portio vaginalis of the cervix contained a black lesion 1.4 cm. in diameter, which surrounded the external os but was not elevated (Fig. 2). This lesion extended into the cervical canal for a distance of 1.4 cm., and on cut section penetrated to a depth of 1 to 2 mm. Microscopic examination revealed numerous cords and nests of polygonal to spindle-shaped cells. The nuclei of these cells showed marked variation in size, shape, and staining qualities, with many mitotic figures. The cytoplasm contained varying amounts of fine granular brown pigment. Several of the tumor nests surrounded isolated segments of cervical glands (Fig. 3). A large portion of cervical epithelium over the lesion was ulcerated. There was no evidence of junctional change in those regions where the tumor had undermined the cervical stratified squamous epithelium.

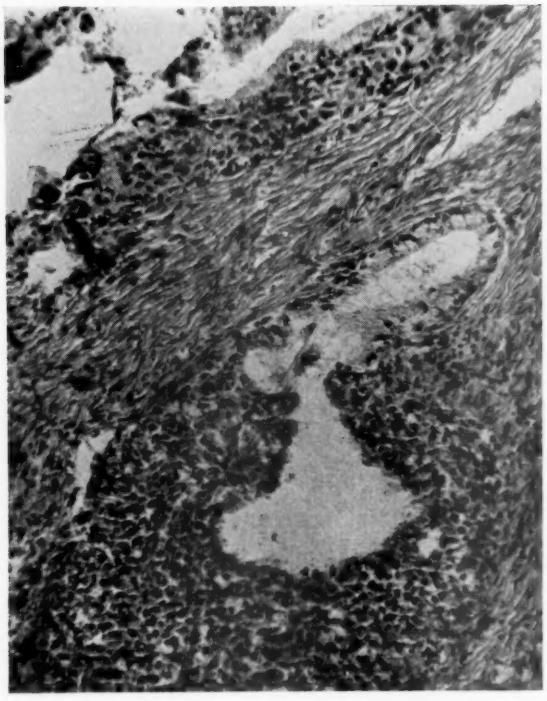

Fig. 3.—Urethral melanoma metastatic to the cervix, undermining and replacing cervical glands (×100; reduced ¼).

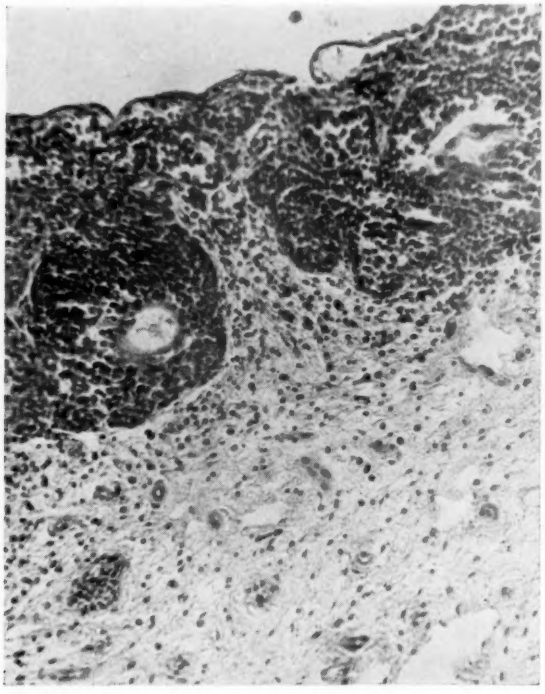

Fig. 4.—Metastatic melanoma in mucous membrane of vaginal introitus (×100; reduced ¼).

The lesion from the vaginal introitus measured 0.7 by 0.3 cm., was slightly elevated, and was dark in color; on section, the color did not appear to penetrate the underlying tissue. The microscopic findings were similar to those of the cervical lesion, and again no junctional change was seen (Fig. 4).

The final pathologic diagnosis was metastatic malignant melanoma in the cervix and vaginal mucosa, probably from the primary melanoma of the urethra.

DISCUSSION

Malignant melanomas comprise 2 to 3 per cent of all malignant neoplasms in the human body. The majority involve the skin, although Allen and Spitz[3] found the primary lesion in the mucosal surfaces in 15.1 per cent of 337 cases. In women, 7 per cent of melanomas develop in the genital area—a region which includes only about 1 per cent of the total body surface. Nevi in the genital region, particularly in the female, are especially prone to become malignant. This fact is not recognized by the medical profession as a whole.

We have been unable to find a report of malignant melanoma of the urethra in the male. Apparently, the lesion develops in this location in women only. The majority, moreover, are beyond the age of 60.

The earliest signs of the tumor are usually slight bleeding and a vaginal discharge. The function of micturition is seldom materially altered, although an occasional patient may complain of dysuria. Clinically, malignant melanoma is most likely to be confused with a urethral caruncle, the gross appearance of the two being practically identical. The first requisite to the correct diagnosis is the suspicion of a malignancy from the clinical findings. A biopsy and examination of the specimen by the pathologist are then in order.

In the experience of Allen and Spitz,[3] malignant melanomas of the female genitals carry a poor prognosis; only one of their eighteen patients was alive at the time of their report. Our patient is living and well three and one-half years after excision of the primary tumor and one year after excision of the metastatic disease. Although the prognosis is guarded, the period of survival thus far seems to have almost set a record.

So far as we could determine from the literature, no other cases of melanoma of the female genitals with metastasis to the cervix have been reported. It is believed that the cervical metastasis may have developed from a local implantation on an area of erosion or ulceration at one of the operations for removal of the urethral lesions. Or, it is possible that metastasis may have taken place via the lymphatics, since the urethra, vagina, and cervix have a closely integrated lymphatic drainage. At the time of laparotomy, however, inspection of the pelvic lymph nodes revealed no abnormality.

SUMMARY AND CONCLUSIONS

1. Primary malignant melanoma of the female urethra, although seldom observed, is nevertheless to be considered in the presence of any tumefactive lesion of this area.

2. Closer attention to the discovery and excision of all pigmented growths in the region of the female genitals would no doubt serve to prevent malignant melanomas and to alter to some extent the almost universally fatal prognosis of those already developed.

3. That the period of survival may at times be prolonged by excision of such lesions is illustrated by the case reported herein. The patient has survived three and one-half years since removal of the original growth and is still in good health.

4. To compound the rarity of the lesion is the fact that our patient had metastases to the cervix and vulvar mucous membranes.

REFERENCES

1. Long, G. C., Counseller, V. S., and Dockerty, M. B.: Primary Melano-epithelioma of the Female Urethra: Review of the Literature; Report of Three Cases, J. Urol. **55**: 520 (May) 1946.
2. Savran, J., Sayer, E. A., and Schradiack, C. E.: Primary Malignant Melanoma of the Female Urethra, Am. J. Surg. **75**: 743 (May) 1948.
3. Allen, A. C., and Spitz, S.: Melanoma: Diagnosis and Prognosis, Cancer 6: 1 (Jan.) 1953.

ACUTE SUPPURATIVE APPENDICITIS WITH PERFORATION RESULTING FROM METASTATIC CARCINOMA, PRIMARY IN THE KIDNEY

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HEREIN is reported a case of carcinoma of the kidney which had metastasized to the appendix, leading to appendicitis with resultant perforation and peritonitis. A search of the literature of the past twenty years failed to uncover a single incident similar to this one. Goldfarb and Zuckner[1] reported a case of inoperable gastric carcinoma with metastasis to the appendix culminating in appendicitis and perforation, which was recognized and treated successfully. An extensive search of the literature by these authors revealed only one case similar to their own, reported by M. C. Oldfield.[2] The latter concerned a 44-year-old woman who had submitted to radical mammectomy for carcinoma three years, eight months previously. Metastasis to the appendix from the original lesion led to perforation. Goldfarb and Zuckner stated that they could locate no other case reports in the American or foreign literature comparable to these two, although there were case reports of metastasis to the appendix without the development of appendicitis.

We found no cases of appendiceal metastasis from renal carcinoma, although Starr and Miller[3] reported one of solitary jejunal metastasis one year after nephrectomy for renal-cell carcinoma (clear-cell carcinoma). Starr and Miller pointed out that renal carcinomas metastasize most commonly to bone, brain, and lungs and sometimes to the skin, gall bladder, bile ducts, corpora cavernosa, epididymis, bowel, pancreas, thyroid gland, pericardium, heart, mediastinum, seminal vesicles, external auditory meatus, and phalanges. There is no mention of metastasis to the appendix.

CASE REPORT

A white woman 72 years of age had consulted a number of doctors with varying complaints since 1939, none of which appeared to be related to the present illness until November, 1952. In the process of investigation for abdominal pains, a mass was palpated in the right upper quadrant. Excretory pyelography was performed, and because the findings were suggestive of a tumor mass in the right kidney, she was referred to Urology. A study of these films revealed a large filling defect in the right kidney with compression of all the calyces and considerable elongation of the pelvis. The filling defect seemed to be a rounded mass about 10 cm. in diameter with calcification in the periphery. Upon careful questioning of the patient, it was concluded that the tumor mass was asymptomatic.

Retrograde pyelography was performed. Indigo-carmine excretion suggested deficient function of the right kidney, particularly as compared to the left. On Nov. 25, 1952, a right nephrectomy was performed. The entire renal mass with attached capsule of Gerota was freed down to the pedicle. The pedicle was found firmly attached to the

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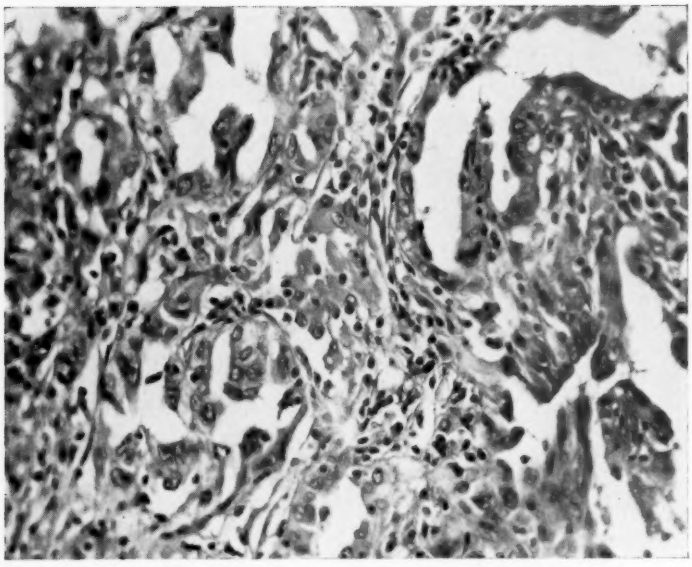

Fig. 1.—Microscopic section of the better-preserved area of original kidney tumor showing the characteristics of so-called pale-cell carcinoma. (×360; reduced ¼.)

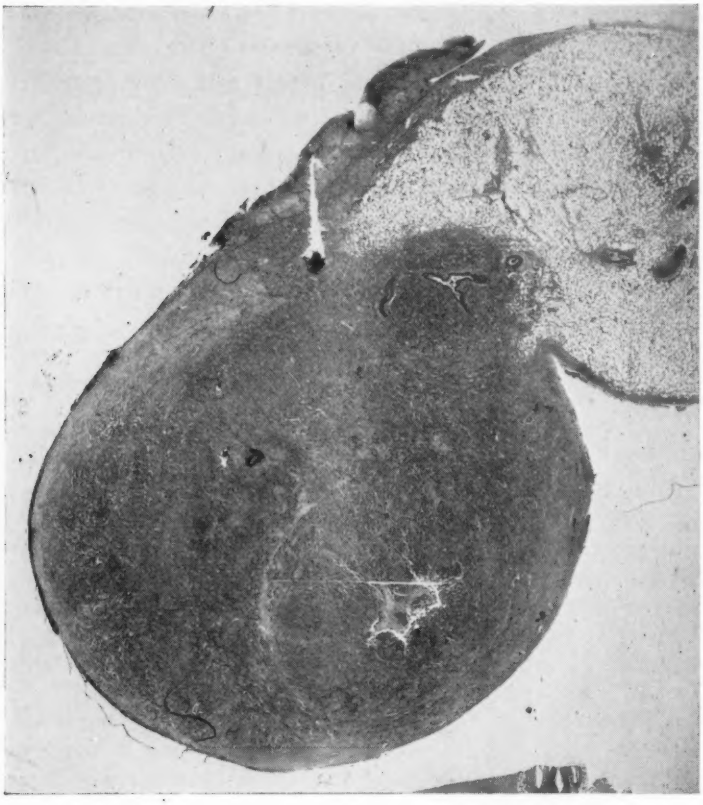

Fig. 2.—Microscopic section of cross section of appendix through the tumor-bearing area. (×4½.)

posterior parietes and the vena cava. By painstaking dissection the tumor mass was freed from the vena cava. A small perforation occurred in the vena cava, but this was readily controlled by packing. At this time it was discovered that the tumor involved both the vena cava and aorta. Tumor tissue could be found to traverse the midline of the body. It was imminent that tumor tissue would be left behind, but the right kidney with its tumor and the attached capsule of Gerota was successfully removed.

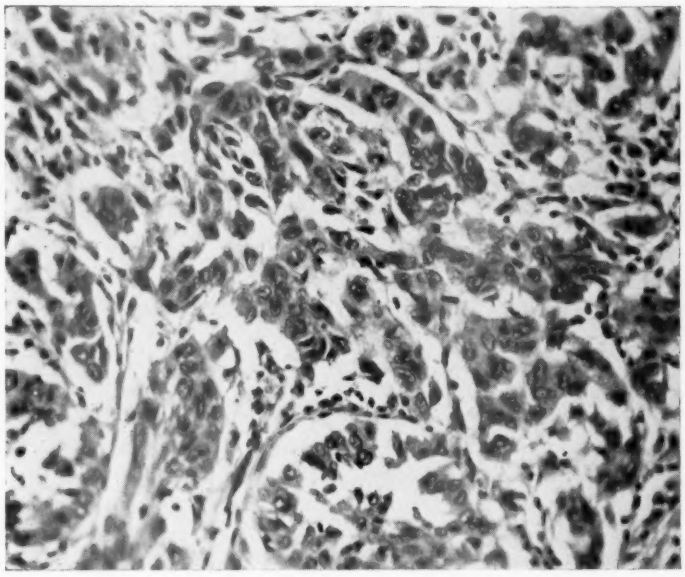

Fig. 3.—Microscopic section of the tumor nodule within the appendix showing the characteristics of so-called pale-cell carcinoma and essentially similar to Fig. 1. (×360; reduced ¼.)

Pathologic Report.—The kidney specimen weighed 292 grams, measuring 14 by 9 by 7.5 cm. The cut surface showed a large, firm predominantly gray tumor mass measuring 10 cm. in maximum diameter. This occupied the middle two-thirds of the kidney, distorting the renal pelvis and displacing it anteriorly. In the central portion of the tumor there was a large circumscribed area of tumor degeneration and necrosis, measuring 5 cm. in diameter. Near the upper calyx there was a small area on the renal pelvic mucosal surface where the tumor had eroded.

Microscopic examination was made of three large representative sections showing a somewhat variable histologic picture. The better-preserved portions showed tumor tissue composed of closely grouped epithelial tumor cells arranged in disordered glandular formations and separated by fibrous stroma. The tumor cells varied in size and shape. The nuclei were hyperchromatic. Some were pleomorphic and showed the classic cytologic features of malignancy, including mitotic figures. In a few areas the epithelial tumor cells had vacuolated cytoplasm, and here they bore some resemblance to the type of cell seen in so-called clear-cell carcinoma of kidney (Fig. 1). There were scattered large areas of tumor degeneration and necrosis. There was also much irregular fibrosis with inflammatory cellular infiltrate, which distorted the tumor pattern. Adjacent to the central zone of necrosis, there were several calcareous deposits. There was rather marked degeneration, distortion, and replacement fibrosis of the included renal parenchyma adjacent to the tumor.

Diagnosis was adenocarcinoma of the right kidney with areas of degeneration, necrosis, and associated inflammation.

The patient was discharged from the hospital on Dec. 7, 1952, convalescence having been satisfactory, albeit rather slow. That pain of which she complained intermittently

for some years continued to trouble her after discharge. When seen four months later the patient appeared to be definitely improved. She resumed most of her usual activities.

On Sept. 13, 1953, the patient consulted an orthopedist, complaining that she was unable to bear weight on the right thigh after slipping while getting up from a chair. Roentgenograms taken for possible fracture were negative. The diagnosis was sprain with possible muscle tearing. The patient insisted upon hospitalization. Within forty-eight hours after admission, the patient started having more abdominal pain with nausea and vomiting with rising temperature. On three prior hospital admissions and on at least one occasion when consulting doctors in the Group, the patient stated that she had had an appendectomy. Later her husband volunteered the information that twenty years prior to the present, the patient had had pelvic surgery, at which time she was told that her appendix had been removed. Knowing the extensive tumor involvement of the great vessels of the abdomen at the time of the nephrectomy, the attending surgeon felt that her present symptoms were a reflection of this condition, and the patient was given opiates for relief. On September 24 the patient expired, and a post-mortem examination was carried out.

The pertinent findings follow.

The omentum and all the organs of the abdomen were covered with a fibrinous exudate.

The left adrenal contained a nodule of metastatic adenocarcinoma.

The right kidney was surgically absent, as were the uterus, tubes, and ovaries.

The cecum was firmly bound in the right lower quadrant. Behind the cecum surrounded by a pocket of purulent fluid lay the appendix covered with fibrinous exudate. Five centimeters distal to its junction with the cecum there was a grayish, firm tumor mass 1.2 cm. in diameter. Cut section revealed this tumor mass to be solid and obliterating the lumen of the appendix. Distal to this, the appendix was dark reddish gray and friable, and 0.5 cm. below the tumor there was a ragged-edged perforation measuring 1.5 cm. in diameter.

Anterior to the vertebral column extending from the insertion of the diaphragm to 3 cm. below the bifurcation of the aorta was a matted tumor mass which encased the aorta. Cut surfaces showed numerous enlarged matted lymph nodes, obviously the site of tumor metastases. Microscopic examination showed lymph node architecture almost completely replaced by metastatic adenocarcinoma, and the fatty tissue adjacent was also infiltrated with tumor. Included in the section is a segment of abdominal aorta.

The section from the distal portion of the appendix showed all layers of its wall diffusely infiltrated with the products of an acute suppurative inflammatory process, and included in the section was the channel of perforation. Another section taken to include the tumor nodule presented the histology of adenocarcinoma (Figs. 2 and 3). The metastatic tumor nodule replaced almost the entire wall of the appendix and markedly constricted the lumen. A single mucosal gland identified the position of the lumen, which appeared as a narrow slit. The outer portion of the muscular tunic of the appendix could be identified at the periphery.

SUMMARY

1. A report of metastasis from renal carcinoma to the appendix with resultant appendicitis, perforation, and peritonitis is presented.

2. This appears to be the first case of this kind to be reported.

REFERENCES

1. Goldfarb, A., and Zuckner, J.: Acute Suppurative Appendicitis With Perforation Resulting From Metastatic Carcinoma. Report of a Case, SURGERY **29**: 137-141, 1951.
2. Oldfield, M. C.: Individual Resistance to Malignant Disease, Brit. M. J. **2**: 153-155, 1946.
3. Starr, A., and Miller, G. M.: Solitary Jejunal Metastasis Twenty Years After Removal of a Renal-cell Carcinoma. Report of a Case, New England J. Med. **246**: 250-251, 1952.

COEXISTENT VOLVULUS OF THE SPLENIC FLEXURE AND CECUM

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IN A recent report, Buenger[1] described two cases of volvulus of the splenic flexure of the colon, believed to be the first such cases recorded. His review of the American and European literature failed to disclose any other reports of this condition.

Volvulus of the cecum has long been considered one of the rarer causes of intestinal obstruction. In 1953, Figiel and Figiel[2] collected 447 cases from the literature and added twenty-four new cases. There have been several additional reports in the brief period since their review. In one of these, Wilson and associates[3] emphasized that volvulus of the cecum may be initiated by partially obstructive lesions of the left colon. Four of their eight patients had coexisting lesions of the left colon (three carcinomas; one benign stricture). These partially obstructing lesions were believed to have been the immediate precipitating factor leading to distention of the cecum, which in turn twisted on the abnormally long mesentery. They pointed out that this feature had not been adequately stressed previously and recommended investigation of the left colon in any case of volvulus of the cecum after the acute problem has been remedied.

In the case described here, volvulus of the cecum was relieved by deflation and detorsion six days after a laparotomy performed elsewhere failed to disclose the nature of the intra-abdominal lesion. Subsequent study of the left colon disclosed a chronic volvulus of the splenic flexure causing partial obstruction. The splenic flexure was resected and the cecum found to be well fixed in its normal position. This is apparently the first instance in which volvulus of the cecum and the splenic flexure of the colon existed in the same patient and the first reported instance in which resection of the splenic flexure was carried out for volvulus.

CASE REPORT

The patient, a 19-year-old white man, became acutely ill on the evening of May 6, 1954, complaining of intermittent cramping, lower abdominal pain. Eight hours after onset, the pain became much more severe and he began vomiting frequently. He was then admitted to a small dispensary, where it was noted that the abdomen was "rigid with guarding, with severe pain localized in the right lower quadrant." A blood count disclosed 20,000 white blood cells per cubic millimeter with 91 per cent neutrophils and 9 per cent lymphocytes. The patient stated that he had never previously experienced any similar symptoms, and his history was entirely negative for abdominal complaints of a chronic or vague nature; constipation was denied. The past history was negative; he had

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not had any abdominal operations. A clinical diagnosis of acute appendicitis was made and an emergency laparotomy performed via a right lower rectus incision. The operator noted a moderate amount of serosanguineous fluid and described the small bowel as inflamed but not distended. The cecum and appendix could not be located. After the incision was extended upward, it was reported that the terminal ileum and cecum were in a "retroperitoneal pocket in a right gutter." It was concluded that the primary cause of the patient's complaints was an acute gastroenteritis with the incidental finding of an intraperitoneal hernia due to an anomaly, and the operative procedure was terminated.

Fig. 1.—Erect scout film showing dilated cecum filling left upper quadrant and some distended loops of small bowel with fluid levels in lower abdomen.

A Levin tube was inserted for gastric suction for three days, after which it was removed as the patient had passed some gas per rectum. On the fourth postoperative day, the abdomen became distended, more so in the left upper quadrant where the patient also noted pain. A gastric tube was reinserted. A scout film of the abdomen was stated to disclose "dilatation of the colon in the left upper quadrant" and the stomach was displaced medially. On the next day the gastric tube was again removed. After the patient vomited 500 c.c. of green fluid, a tube was reinserted. The following day, May 13, a scout film disclosed "increased distention of the large bowel," and the patient was transferred to the U. S. Naval Hospital, Yokosuka, Japan.

Examination disclosed an alert young man who did not appear acutely ill. His blood pressure was 110/80 mm. Hg. His pulse was 94 and his respiratory rate 20 per minute. The oral temperature was 99.4° F. General examination was negative except for the abdomen, which was uniformly distended, tense, and tympanitic, the latter finding being more marked in the left upper quadrant, where the patient complained of cramping

pain at frequent intervals. There was moderate direct tenderness over the entire abdomen; no rebound tenderness was present. There was a sutured, healing incision over the right lower rectus muscle. Auscultation revealed occasional peristaltic rushes which were not high pitched. A blood count disclosed 24,700 white blood cells per cubic millimeter with 2 per cent juvenile forms, 13 per cent band forms, 71 per cent polymorphonuclear neutrophils, and 14 per cent lymphocytes; there were 4,420,000 red blood cells per cubic millimeter and 13 Gm. hemoglobin per 100 c.c. Urinalysis was normal. Flat and erect scout films of the abdomen disclosed a greatly distended loop of intestine filling most of the left upper quadrant, lying immediately under the left diaphragm, and, in addition, several moderately distended loops of small bowel containing fluid levels (Figs. 1 and 2). It was concluded that emergency surgical intervention was indicated promptly; an exact preoperative diagnosis was not ventured.

Fig. 2.—Chest film on same date showing dilated cecum in more detail.

Under general endotracheal anesthesia, the previous incision was reopened. A moderate amount of serosanguineous peritoneal fluid was aspirated. The omentum was found to be adherent to the distal jejunum, causing a kink with complete obstruction. The proximal jejunum was moderately distended while the distal small bowel was collapsed and ribbonlike. The recent omental adhesion was readily separated with a finger, disclosing a 1 cm. diameter necrotic area in the jejunal wall at its point of attachment; this area was protected with a moist sponge. Manual exploration disclosed a greatly distended

cecum in the left upper quadrant. After upward extension of the incision, the cecum still could not be delivered with safety, as its stretched wall appeared very thin. An elongated, noninflamed appendix was delivered and removed. A suction tip was inserted through a purse-string suture around the unligated appendiceal base and the cecal contents, chiefly gas, were aspirated. The purse-string suture was tied after removal of the suction tip. It was then possible to reduce a clockwise twist of 540 degrees of the mesentery of the terminal ileum and cecum. There were no areas of questionable viability in the cecum or ascending colon. However, it was not felt advisable to attempt any type of cecopexy due to marked thinning of the cecal wall. A suction tip was introduced through the small area of necrosis in the wall of the jejunum and the proximal small bowel was decompressed; the perforation was then closed with interrupted serosal sutures.

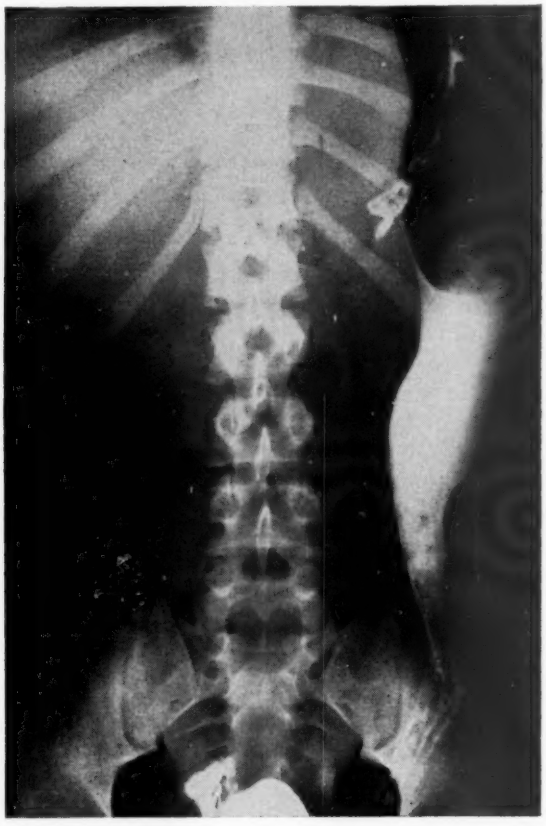

Fig. 3.—Evacuation film after first barium enema disclosing minimal barium in the transverse colon, which is narrowed at its point of entry into the moderately dilated splenic flexure.

Further exploration disclosed the transverse colon and descending colon to be in their normal locations, empty, and almost ribbonlike. The splenic flexure was not visualized. However, after the cecum was delivered from the left upper abdomen and the proximal jejunum deflated, there was no other distended segment of bowel present. There was no "pocket" of peritoneum in the right gutter or internal hernia.

Postoperatively, gastric suction was maintained and opiates were administered regularly in an effort to keep the bowel quiescent and possibly facilitate fixation of the cecum in the right lower quadrant by adhesions. The patient had two bowel movements on the third day after operation; the gastric tube was then removed and oral feedings were started. On the next day, a distended tympanitic mass was noted in the left upper

quadrant and a scout film disclosed a dilated segment of colon beneath the left diaphragm. It was feared the cecum had again undergone rotation, perhaps only 180 degrees. Although the left upper quadrant distention persisted, the patient's clinical course was uncomplicated; he was able to eat a regular diet and had normal bowel movements.

Fig. 4.—Evacuation film after second barium enema showing dilated splenic flexure filling the entire left subdiaphragmatic space.

A barium enema examination performed on May 25, 1954, disclosed distention of the splenic flexure and proximal ascending colon with almost complete obstruction to the flow of barium into the distal transverse colon. The latter appeared to enter the dilated splenic flexure obliquely on its posterior surface (Fig. 3). A second barium enema examination performed June 9, 1954, disclosed increase in the distention of the splenic flexure (Fig. 4). On one of the evacuation films, a point of narrowing was demonstrated in the descending colon just distal to the marked dilatation (Fig. 5). It was believed this represented the distal point of torsion, which had been reduced by the pressure of the enema. There was no evidence of obstruction in the colon distal to this point, and sigmoidoscopic examination was negative to 25 cm. Barium was administered orally on June 14 and its course followed. The cecum was found to be in the right lower quadrant, still moderately dilated; there was some delay in passage of the barium into the splenic flexure, which allowed visualization of the distal transverse colon (Fig. 6).

Following detorsion of the cecum, the patient remained asymptomatic until June 23, 1954, when he noted intermittent abdominal cramps and moderate distention. Roentgenograms disclosed moderate distention of the small bowel and right and transverse colon. This subsided within forty-eight hours without any specific treatment. A decision was then made to carry out definitive surgical treatment and the bowel was prepared. On

July 2, 1954, a left upper paramedian incision was made and abdominal exploration carried out. The cecum was found to be immobile, being well fixed by adhesions in the right lower quadrant. The splenic flexure was dilated up to 15 cm. in diameter. It could not be delivered into the incision until some thick peritoneal bands connecting its posterior surface to the lateral portion of the left diaphragm were sectioned. These bands produced a twisting of the splenic flexure, causing the proximal descending colon to become obstructed due to the waistlike narrowing at the point of axial torsion and displacing the distal transverse colon posteriorly, flattening the bowel at its point of entry into the dilated splenic flexure. The distal transverse colon, the splenic flexure, and the proximal descending colon were resected and an end-to-end anastomosis was performed. The postoperative course was uncomplicated and the patient has remained free of any symptoms. Histologic examination of sections taken from all portions of the resected specimen disclosed the normal number of myenteric plexuses. A barium enema examination performed three weeks after operation disclosed a wide stoma at the site of anastomosis with moderate dilatation of the right and transverse colon still present.

Fig. 5.—Marker indicates point of narrowing in proximal descending colon corresponding to site of axial torsion seen at operation.

COMMENT

It is difficult to explain the absence of symptoms prior to the acute onset. However, the patient was an intelligent and observing person and the history was considered reliable. There seems little doubt that the volvulus of the cecum existed for almost one week before it was reduced. The patient was most fortunate that circulatory impairment and gangrene did not occur. At

the time of the second laparotomy and detorsion of the cecum, the situation was further complicated by the complete jejunal obstruction secondary to the recent adhesion. Resection of the right colon, recommended by Wilson and co-workers,[3] conditions permitting, was not considered advisable under these circumstances. The subsequent course substantiated this decision, as the cecum became fixed in its normal location. In addition, right colectomy would not have corrected the primary difficulty, the volvulus of the splenic flexure, which was not recognized until x-ray studies were performed later.

Fig. 6.—One month after detorsion of the cecum, it is seen to be moderately dilated and in a normal position. Twenty-four hours after administration of the barium meal, none of the contrast medium is seen to have entered the splenic flexure and the distal transverse colon is well outlined.

The peritoneal bands causing the torsion of the splenic flexure appeared to be congenital in origin rather than inflammatory. A torsion in the long axis of the proximal descending colon was produced by these bands, the resulting obstruction causing marked dilatation with hypertrophy of the muscular coats. The distal transverse colon was actually not involved in the volvulus. In contrast, in the two cases described by Buenger,[1] the distal transverse colon and proximal descending colon appeared to be twisted on their mesentery, forming the type of volvulus usually seen in the sigmoid colon.

When deflation of a distended cecum that has undergone volvulus is indicated to facilitate its delivery and detorsion, the method used in this case

is recommended provided the appendix is present and can be adequately exposed. With care, the procedure can be carried out without contamination. Inversion of an unligated appendiceal stump is the method of choice of many surgeons in performing a routine appendectomy.

It is possible that simple lysis of the peritoneal bands causing the volvulus of the splenic flexure would have been adequate treatment. This method was successfully used in one of the cases described by Buenger.[1] However, it was felt that resection added minimal additional risk in this healthy young man and would give the greatest chance for permanent relief. In addition, there was the remote possibility that an unusual form of Hirschsprung's disease existed since a point of distal obstruction could not be demonstrated with complete certainty. The findings at operation and histologic study of the resected portion of colon excluded this possibility.

SUMMARY

The case of a 19-year-old man is described in which a chronic volvulus of the splenic flexure of the colon causing partial obstruction is thought to have been the precipitating factor responsible for volvulus of the cecum. Subsequent to detorsion of the cecum and roentgenographic studies of the colon, resection of the splenic flexure was performed with relief of symptoms. This is believed to be the third recorded case of volvulus of the splenic flexure of the colon and the first instance in which this condition coexisted with volvulus of the cecum. Roentgenographic demonstrations of this unusual condition are presented.

REFERENCES

1. Buenger, R. E.: Volvulus of the Splenic Flexure of the Colon, Am. J. Roentgenol. **71:** 81-83 (Jan.) 1954.
2. Figiel, L. S., and Figiel, S. J.: Volvulus of the Cecum and Ascending Colon, Radiology **61:** 496-515 (Oct.) 1953.
3. Wilson, H. E., Desforges, G., Dunphy, H. G., and Campbell, A. J. A.: Volvulus of the Cecum: Emphasis on Possible Predisposing Lesions of the Left Colon, Arch. Surg. **68:** 593-604 (May) 1954.

CARCINOMA OF THE SIGMOID METASTASIZING TO THE ANUS BY THE MUCOSAL ROUTE

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THE metastasis of tumor cells from one portion of the gastrointestinal tract to another through the lumen of the bowel is an infrequent occurrence. This type of metastasis has been called implantation metastasis, mucosal metastasis, and drop metastasis. In a recent case reported by Guiss,[3] a primary tumor of the sigmoid metastasized to a fistula in ano. I should like to report a similar unusual case where a sigmoid carcinoma metastasized into an anal crypt.

CASE REPORT

A 52-year-old Negro woman was admitted to the University of Virginia Hospital on Feb. 4, 1954, complaining of rectal bleeding for two years. Two months prior to admission, this bleeding became more pronounced. The blood was usually bright red in color. Occasionally, there had been some clots, and recently, she had noted the appearance of a mass near the anus, which she thought was a hemorrhoid. She consulted her local physician, who referred her to a surgeon. A proctoscopy and a biopsy of the anal lesion were performed. The biopsy was reported adenocarcinoma of the anus. She was then referred to the University Hospital for treatment.

Examination revealed a moderately obese Negro woman in no acute distress. There was a mild hypertension but no evidence of cardiac disease. The abdominal examination revealed a large abdomen without tenderness, masses, or muscle spasm. Pelvic examination was unremarkable. At the anus, just outside the external sphincter, an ulcerating tumor 2 cm. in diameter was found. On digital examination, this mass was found to invade the external sphincter and the lower 2 cm. of the rectal mucosa. Proctoscopy showed a normal rectum up to six inches. A biopsy was taken and reported as adenocarcinoma, grade 2.

Admission laboratory work was within normal limits. Chest roentgenogram was normal.

It was felt that this woman had a low-lying rectal carcinoma which had invaded the sphincter and anal skin. She was then prepared for large-bowel surgery. At exploration, a large, ulcerating, annular tumor in the sigmoid colon was found at the brim of the pelvis. There were numerous lymph nodes along both iliac arteries and the aorta. A segment of small bowel, approximately 20 cm. from the ileocecal valve, was adherent to the tumor. The uterus, tubes, and ovaries were normal. There were no tumor nodules or implants on the pelvic peritoneum. The rectum beneath the tumor mass was freely movable, and no tumor could be felt in the rectum itself. There was no evidence of any liver metastases. A radical abdominoperineal resection of the sigmoid and rectum with ligation of the inferior mesenteric artery and resection of the involved segment of small bowel was performed.

Examination of the specimen after removal proved to be most interesting (Fig. 1). The large tumor mass in the sigmoid colon appeared to be the primary tumor, whereas the

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tumor that had presented at the anus appeared to be a drop metastasis which had imbedded itself in an anal crypt (Fig. 2.). The final pathology report was mucoid adenocarcinoma of the rectosigmoid, grade 3, with metastasis to the anorectal junction. Two lymph nodes in the specimen showed metastases. There was one lymph node at the level of the tumor and one distal to it (Fig. 3.). Thirty-nine lymph nodes, including all of those from the most proximal point of the dissection, were free of tumor.

This patient's postoperative course was uneventful. She was examined nine months following this surgery, and all wounds were well healed and there was no evidence of any residual or recurrent tumor.

Fig. 1.—Appearance of specimen after removal. The bowel has been opened along the antimesenteric border to show the sigmoid lesion and the anal metastasis.

DISCUSSION

The usual methods of metastasis are by the lymph channels, by the blood stream, and by implantation. The common method of implantation metastasis occurs by mechanical transport across serous cavities, as, for example, seeding of the peritoneum with multiple nodules of a primary ovarian tumor or the

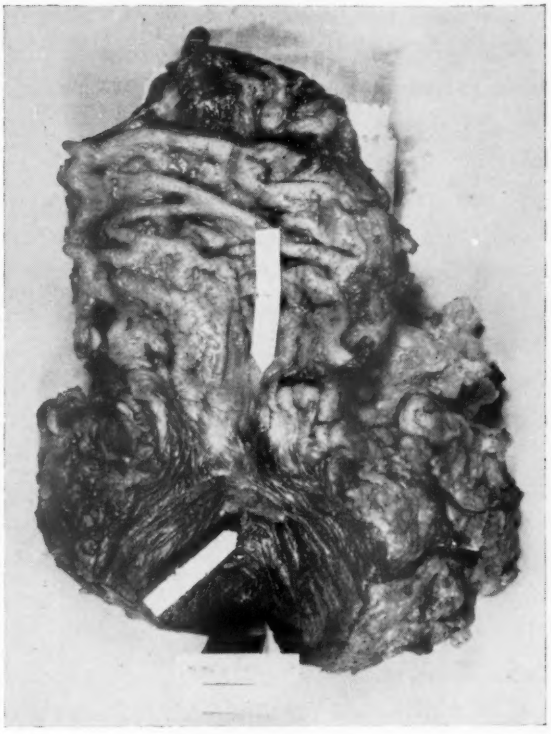

Fig. 2.—Closer view of the anus and lower rectum showing the metastatic lesion at the anus.

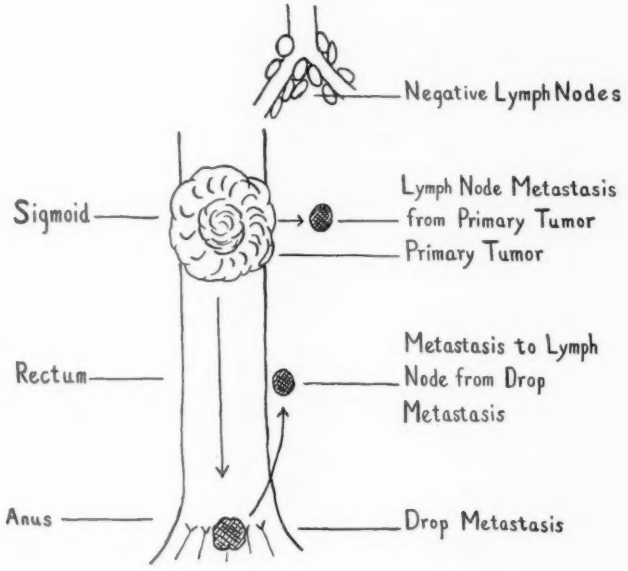

Fig. 3.—Diagram of Fig. 1 illustrating the route of the metastases.

growth of tumor cells within serous exudates and transudates. We should not forget, as pointed out by Cole,[2] the danger of implantation of desquamated tumor cells at the suture lines and in the incisions of colon resections.

Willis[5] stated that it is inherently improbable for tissue grafts to take on intact surfaces bathed by digestive juices and mucus and rich in bacteria, and that we must apply the greatest stringency in judging alleged instances of tumor implantation in the alimentary canal. He noted that critical examination of such cases shows that the supposed implants should be attributed either to multiple primary tumor formation, or to transcelomic or vascular metastases.

Certainly the implantation of tumor cells on intact mucosal surfaces must be rare. The presence of tumor cells within the lumen of the bowel, however, has been frequently demonstrated, and Wisseman[6] has advocated a cytologic technique in the diagnosis of cancer of the descending colon, sigmoid, and rectum. Perhaps a break in the mucosal surface is necessary before implantation occurs. In the case reported by Guiss,[3] the tumor cells were implanted within a fistula in ano. In this case report, the implantation occurred either in an anal crypt, or a fistula in ano, although there was no history of such a fistula.

Rössle,[4] in an excellent review of this subject, reported a number of instances of metastases of malignant tumors by the mucosal route. He reported a case of a metastatic renal tumor that metastasized to the mucosa of the ureter. In another of his cases, a primary cancer of the cardia showed over 100 miliary metastases of the mucosa in which neoplastic cells penetrated into the stomach glands. Rössle attributed this type of metastasis to the fact that the neoplasms are of an extremely high grade of malignancy and that their cells can destroy normal mucosal epithelium on contact. Such a destructive growth must, consequently, be regarded as the highest grade of malignancy. The fact that this grade is seldom reached in human tumors explains the rarity of metastasis by the mucosal route.

There are no other unusual features in this case or in the case reported by Guiss that suggest an unusual high grade of malignant tumor. In both cases, however, we have evidence that the implantation occurred in an area where there was a break in the epithelium.

Another aspect of this case is the single metastatic lymph node between the primary lesion and the anal lesion (Fig. 3). According to Ackerman,[1] retrograde lymphatic metastases do not occur in lesions of the colon and rectum until the proximal lymphatics and lymph nodes are filled and blocked with tumor cells. If this be true, then the metastatic tumor cells in this lymph node must have come from the anal lesion, as only one of the thirty-four proximal lymph nodes contained tumor cells.

SUMMARY

1. A case of adenocarcinoma of the sigmoid colon with drop metastasis to an anal crypt treated by abdominoperineal sigmoidoproctectomy is reported.

2. There is some evidence to show that the mucosal or drop type of metastasis will occur only if there is a break in the epithelium prior to implantation.

3. Such cases must be more common than has been reported, and by the study of more cases we may be better able to explain their occurrence.

REFERENCES

1. Ackerman, L. V., and Regato, J. A.: Cancer; Diagnosis, Treatment, and Prognosis, St. Louis, 1947, The C. V. Mosby Company, p. 582.
2. Cole, W. H.: Recurrence in Carcinoma of the Colon and Proximal Rectum Following Resection for Carcinoma, Arch. Surg. **65:** 264 (Aug.) 1952.
3. Guiss, R. L.: The Implantation of Cancer Cells Within a Fistula in Ano. A Case Report, SURGERY **36:** 136 (July) 1954.
4. Rössle, R.: Ueber die Metastasierung bösartiger Geschwülste auf dem Schleimhautwege und ihre Bedeutung für das Problem der Malignität, Arch. path. Anat. **316:** 501, 1949.
5. Willis, R. A.: Pathology of Tumours, St. Louis, 1948, The C. V. Mosby Company, p. 187.
6. Wisseman, C. L., Jr., Lemon, H. M., and Lawrence, K. B.: Cytologic Diagnosis of Cancer of the Descending Colon and Rectum, Surg., Gynec. & Obst. **89:** 24 (July) 1949.

A CASE REPORT OF TWO SPHERICAL DUPLICATIONS OF THE SECOND PORTION OF THE DUODENUM IN A 54-YEAR-OLD PATIENT

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IT IS our purpose to report a case which suggests that duplication of the duodenum should be considered in the differential diagnosis of massive upper gastrointestinal hemorrhage or chronic intestinal obstruction. Familiarity with this entity permits surgical repair by a simple operation avoiding a high mortality and morbidity.

CASE REPORT

E. C. is a 54-year-old white man, who was admitted to the Minneapolis Veterans Administration Hospital on Sept. 30, 1953, because of epigastric pain and vomiting. The history on admission revealed that for the past eight or ten years he had had episodes of pain which had recurred once or twice a year. The present episode began two months prior to admission. He had had a burning epigastric sensation which radiated to the upper back and a sensation of a lump between his shoulder blades. These discomforts usually began shortly after the evening meal, and would frequently culminate in vomiting, which would relieve the distress. The patient had been on ulcer management without relief. His bowel habits were normal, and there had been no jaundice or hematemesis.

Past Medical History.—The patient stated that he had always suffered from "stomach trouble." As an infant, he had vomiting after each feeding. Feedings at frequent intervals throughout the day and night resulted in less vomiting and in a slow gain in weight. For the first seven years of life the patient was able to take very little food except milk and bread. Any amount of solid food would cause him to vomit. After the age of 7, the vomiting episodes became less frequent and severe. In 1944 he had right upper quadrant postprandial pain without vomiting. Roentgenogram was reported as showing a deformity of the duodenal cap. During subsequent admissions, he continued to experience similar distress and was studied on several occasions without a definite conclusion being reached. Cholecystograms were negative. In 1947 he experienced vomiting and pain similar to those described on the present admission and responded to symptomatic treatment. At that time cholecystogram showed a poorly functioning gall bladder. The gastrointestinal series showed a large duodenal bulb, but it was considered otherwise negative. In 1949 a gastrointestinal series was reported as showing duodenal irritability, and the symptoms responded to symptomatic management. In December, 1952, a gastrointestinal series showed a narrowing of the second portion of the duodenum which could not be explained. The twelve-hour night gastric aspiration was 1,040 c.c.

Physical Examination.—The patient did not appear to be acutely ill, but did complain of epigastric distress. Examination of the abdomen revealed a nontender liver palpable one to two fingerbreadths below the costal margin. No fluid was noted in the abdomen and it did not appear to be distended. The spleen and kidneys were not palpable and there were no palpable tumor masses. There was slight tenderness in the epigastric region but no muscle spasm or rigidity.

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Hospital Course.—The patient was given a bland diet and Banthine. On this regimen he continued to vomit two to three times a day and his diet was eventually reduced to hourly feedings of skim milk. A gastrointestinal series on Oct. 5, 1953, revealed persistent narrowing of the second portion of the duodenum. A twelve-hour night secretion was 700 c.c. After the vomiting was controlled on the skim milk regimen, his diet was gradually increased, and although he again experienced distress and fullness, no further vomiting occurred. He gained fifteen pounds.

At laparotomy on Nov. 9, 1953, two cysts measuring 3 by 3 cm. and 2 by 3 cm. were found in the second portion of the duodenum. These had no communication with the duodenum. The cysts contained a clear mucoid secretion. By their size they nearly occluded the lumen of the duodenum; however, there was no evidence of necrosis of the cysts' walls or scarring of the duodenum. A windowing procedure was performed with an unroofing of the duplication to its widest diameter similar to the method described by Gardner and Hart.[2] The mucosa of the duodenum was sutured to the mucosa of the duplication with interrupted catgut sutures. The postoperative course was uneventful. The patient has been followed for approximately one year without any recurrence of digestive complaints.

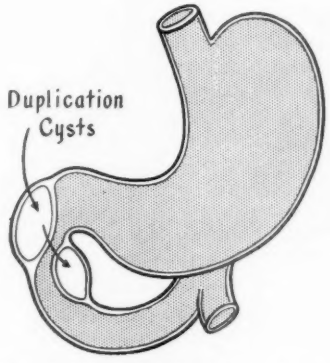

Fig. 1.—Diagram showing the two cysts located in the second portion of the duodenum. They nearly occlude the duodenum by protruding into the lumen from the medial and lateral sides.

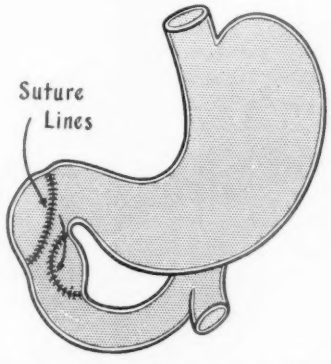

Fig. 2.—Diagram showing the postoperative result of the excision of the intraluminal portion of the cyst. The duplication was unroofed to its widest diameter. The mucosa of the duodenum was sutured to the mucosa of the duplication. Now the duodenal wall is partially formed by the outer wall of the cysts.

Microscopic sections of the septum revealed duodenal mucosa with a small amount of the muscularis present in the deep portion. The mucosa was intact throughout with a moderate lymphocytic and plasma-cell infiltration of the superficial portion of the mucosa. There were many Brunner's glands present. In the mucosal lining of the cyst there were areas of ulceration and marked lymphocytic infiltration with fibroblastic proliferation and scarring throughout the muscular wall.

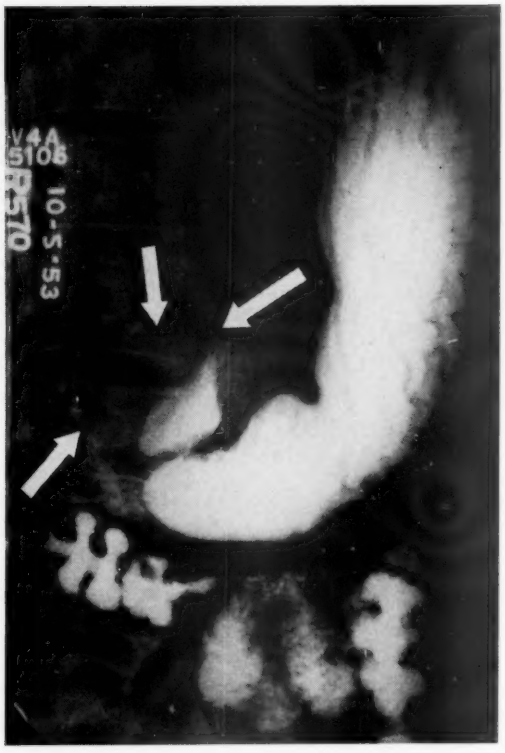

Fig. 3.—Upper gastrointestinal roentgenogram of Oct. 5, 1953, showing the degree of preoperative duodenal obstruction by a lesion of the second portion of the duodenum.

Fig. 4.—Upper gastrointestinal roentgenogram taken Oct. 1, 1954, showing the obstruction of the duodenum to be relieved. The stomach empties rapidly. There is no evidence of ulceration.

DISCUSSION

There are certain features that are characteristic of all duplications. They are contiguous or strongly adherent to some portion of the alimentary canal, have a smooth muscle coat usually of two layers, and are lined by mucosa or epithelium similar to some portion of the gastrointestinal tract.

The microscopic structure bears a striking resemblance to normal bowel, having a mucosa, one or several layers of muscle, and often a well-defined serosa. The lesions are contiguous with the intestinal tract and have a common wall with interlacing muscles.

They may assume a variety of sizes and shapes. They may consist of a small cystic lesion of the size of a bean or pea, or may be massive cystic lesions occupying the greater part of the abdominal cavity. Duplications may be double-barreled structures communicating with the intestine at both ends. Some have been described as cystic structures lying free in the peritoneal cavity, attached only by a thin enteric stock. The spherical lesions are contiguous with some part of the gut, especially the ileum. Moore[6] stated that spherical lesions do not communicate and are usually lined with iliac or colonic mucosa or both. A trained observer examining a specimen of the cystic wall of a duplication may be unable to distinguish it from the normal intestine. Ladd and Gross[5] pointed out that histologically the muscular coats of a duplication are intimately adherent to and at times are microscopically an integral part of the muscular portion of the alimentary canal.

It is important for the surgeon to recognize the pathologic difference between an intestinal duplication and a mesenteric cyst. The latter is lymphatic in origin having a thin wall and can readily be separated from the adjacent bowel.

Fisher[1] stated that the blood supply to a duplication is usually common to the duplication and the contiguous bowel. If a cyst is present, the contents may vary from sterile, mucoid, hemorrhagic fluid, to pus containing colon bacilli.

Samagio[7] reported the incidence of duplication to be the same in males and females, ninety-five per cent of duodenal duplications occur in the concavity of the duodenum, principally in the second and third portions.

Symptoms of Duplication of Duodenum.—The symptoms of a duplication of the duodenum vary with the location of the cyst. Duodenal cysts most frequently simulate pyloric stenosis. Usually projectile vomiting starts at birth or shortly after and it may become persistent. The first abnormality noted may be a tumor mass which has not yet caused symptoms. In the case of duodenal cysts, the mass is usually described as a rather large pyloric tumor. The size of the tumor mass may make the diagnosis of pyloric stenosis unlikely. An abdominal cyst should be suspected when a freely movable or variable mass is palpated in the region of the duodenum. If vomiting and abdominal pain occur, the likelihood that the mass is a duplication is increased. An intravenous pyelogram will differentiate the mass from a kidney lesion.

Usually cysts of the duodenum are noticed during childhood. It should be pointed out that tubelike lesions can encroach upon the adjacent intestine and cause obstruction; the lining may secrete and cause pressure necrosis by distention of the intestine. Often a cyst may become large enough to encroach on the mesenteric blood vessels, causing necrosis, sloughing, and bleeding of the intestine.

Moore and Batterby[6] stated that symptoms caused by duplication rarely lead to a correct diagnosis. The diagnosis is usually an operative one. Moore also believes that palpation is unrewarding except when the duplication is of a large size or has produced intussusception.

Gross, Holcomb, and Farber[4] stated that physical examination often gives important information of the location of the lesion and often may strongly suggest the proper diagnosis. Cysts of the duodenum and jejunum could be palpated in practically all cases. They described the tumor mass as elastic, well rounded, and usually nontender, and except in the duodenum the mass is quite movable in the abdominal cavity. In each of their cases, physical examination revealed the signs of intestinal obstruction.

Roentgenologic Data.—Upper gastrointestinal roentgenograms show the duplication in relationship to the abdominal organs. Duodenal cysts reveal definite evidence of obstruction. Distended loops of bowel in the location of the obstruction give some idea of the level of the lesion. The duplication can be visualized only if it is quite large. It is rare to have barium enter the lumen of a duplication and identify it. Ladd and Gross[5] believe that as much can be learned from a flat plate of the abdomen in the posteroanterior plane as can be determined by a barium gastrointestinal series.

Treatment.—Obviously the treatment of these lesions is surgical. Two important facts are again stressed and these are: first, the duplication and the intestine usually have a common wall at one point and the two cannot be dissected apart with safety; second, the blood vessels may course over the cyst; hence, local removal of the cyst may produce ischemia with necrosis of the intestine. Ladd and Gross believe that total excision of the mass with the adjacent portion of the intestine is the treatment of choice. This is based on the belief that the mass cannot be enucleated without danger of perforation and the danger of leaving an ischemic area.

The treatment of duplication can be resolved into four possibilities: (1) The cyst may be resected together with the adjacent intestine. This is the most practical and most successful form of treatment. (2) Cysts may be marsupialized. Subsequent resection is usually required as the cysts return. (3) Cysts may be changed into diverticula by excising the common wall. A finding of gastric mucosa or pancreatic nests in the wall to be left would contraindicate this procedure. (4) Duplication may be enucleated.

Gardner and Hart[2] suggested that when resection of the lesion is not possible, the procedure of choice is internal drainage of the cyst into the intestinal tract. Drainage may be accomplished by anastomosis between the cyst and the duodenal lumen. In the case of their patient treated by internal drainage, the patient was asymptomatic fifteen months later. The procedure in the pa-

tient we are reporting is similar to that performed by Gardner and Hart. We attempted to create more than a window for drainage. In our case the entire common wall that existed between the cyst and the duodenum was removed to the widest margin of the cyst. It is felt that this treatment is sufficient in the spherical duplications contiguous with the bowel wall and having a common wall with the bowel.

The cause of the high mortality in duplication can be summarized as follows: Most infants with intestinal abnormalities are born prematurely, and are in poor condition for surgery. Often there are other abnormalities present in these infants. Delay in operation and tardy diagnosis contribute to the poor prognosis. Inadequate preoperative and supportive therapy, operative indecision, and unphysiologic operations also contribute to the high mortality.

SUMMARY

A case of a 54-year-old man with two spherical duplications of the duodenum has been presented. The pathology, symptoms, diagnosis, and treatment of duplication of the duodenum are reviewed. Excision of the common wall between the cyst and the duodenum is recommended as a simple procedure when its employment is feasible.

REFERENCES

1. Fisher, H. C.: Duplications of the Intestinal Tract in Infants, Arch. Surg. **61**: 957, 1950.
2. Gardner, C. E., Jr., and Hart, D.: Enterogenous Cysts of Duodenum, J. A. M. A. **104**: 1809, 1935.
3. Glover, D. M., and Barry, F. M.: Intestinal Obstruction in the Newborn, Ann. Surg. **130**: 480, 1949.
4. Gross, R. E., Holcomb, G. W., and Farber, E.: Duplications of the Alimentary Tract, Pediatrics **9**: 449, 1952.
5. Ladd, W. E., and Gross, R. E.: Surgical Treatment of Duplications of the Alimentary Tract: Enterogenous Cysts, Enteric Cysts, or Ileum Duplex, Surg., Gynec. & Obst. **70**: 295, 1940.
6. Moore, T. C., and Batterby, S. J.: Congenital Duplications of the Small Intestine, Surg., Gynec. & Obst. **95**: 558-67, 1952.
7. Samagio, E.: Duplications of the Duodenum; Clinical Aspect and the Roentgenologic Diagnosis, Gaz. méd. port. **5**: 149, 1952.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

A STUDY OF DELIBERATE HYPOTENSION IN ANESTHESIA, WITH SPECIAL CONSIDERATION OF SURGICAL BLOOD LOSS IN COMPARABLE GROUPS OF NORMOTENSIVE AND HYPOTENSIVE ANESTHESIA

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IN RECENT years various techniques have been used to reduce the arterial blood pressure during surgical operations. These techniques, which have been called "deliberate hypotension," "controlled hypotension," or "hypotensive anesthesia," have been adopted with the idea that one or all of the following benefits might be achieved: (1) production of a bloodless field at operation, which would facilitate the surgeon's work and reduce the operating time; (2) a decrease of the amount of blood lost, which would obviate the necessity of blood transfusion with its attendant hazards and expenses; (3) rendering operable those patients who would otherwise be inoperable because of inaccessability of the lesion and the danger of massive hemorrhage.

Although there have been many published reports of operations performed with these techniques, seldom has there been an analysis of the degree to which these goals actually have been attained. The majority of operations reported in the literature could be also safely performed with conventional anesthesia. In an attempt to provide objective data related to the previously listed factors, controlled hypotension was provided for a standardized type of operation for which a control series was readily available, radical mastectomy. In addition, our experience with controlled hypotension for other operations is reported, to define, if possible, the indications, limitations, and complications of this method of management.

GENERAL CONSIDERATIONS

There is evidence that hypotension entails little hazard in the presence of vasodilation and normal circulating blood volume.[1, 2] There is a basic difference[3] between the hypotension resulting from deliberate blood letting,[4] which actually imitates hemorrhagic shock, and that produced by decreasing sympathetic tone to blood vessels either with ganglionic blocking agents[5-8] or with spinal anesthesia.[10, 11] In the former instance (blood letting) progressive com-

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pensatory vasoconstriction leads to tissue ischemia and ultimately, if allowed to persist, to irreversible tissue damage. Vasodilation, on the other hand, probably ensures adequate tissue perfusion, which is evidenced clinically, at least in the periphery, by a warm, dry, and pink skin, dilated veins, and a satisfactory capillary refill time. For these reasons we have chosen to produce hypotension in our study by means of a ganglionic blocking agent, hexamethonium bromide (C_6*) with modification of the technique first described by Enderby.[5-8] Since it is not always possible to lower the pressure to the desired level by mere injection of C_6, the technique includes posturing the patient in such a way that the operative field lies uppermost. This combination lowers the blood pressure and renders the operative field relatively ischemic. Other devices employed to increase the hypotensive effect of C_6 are general anesthetic agents, opiates, and natural curare drugs.

METHOD AND MATERIAL

The basis of this report is provided by the first fifty-three operations performed under controlled hypotension at the Cancer Hospital in Lima, Peru, in 1953 (Table I). Of these, twenty were radical mastectomies (patients Nos. 1 to 20, Table I†), for which a satisfactory control group of twenty operations with normotensive anesthesia was obtained by alternating selection of cases. In the mastectomy group, patients with unusual extension of the breast lesions, with extremes of body weight, and those in whom hypotension below 80 mm. Hg systolic could not be produced are not included in this study. Conditions were maintained as nearly alike as possible in the two groups. Except for the hypotension in the studied group, the anesthetic techniques were the same. Identical surgical techniques were applied to the two groups by the same surgeon and assistant.

Cases No. 23 to 32 of Table I are instances of fairly well-standardized thoracic operations for which there were controls but not with the comparability of those in the mastectomy series. Surgical technique, surgeon, and assistant were also identical in this group.

Finally, Cases No. 33 to 53 of Table I represent operations for which satisfactory controls were not available but which provide a basis for understanding of the over-all problem.

In all operations the degree of facilitation of surgery was estimated by the surgeons. Blood loss was measured[13] by the gravimetric technique first described by Wangensteen[12] in all but the neurosurgical operations.

Patients selected for controlled hypotension had a careful medical checkup including an electrocardiogram before operation. All fifty-three patients were young or middle-aged adults. Patients with anemia, obviously deficient blood volume, abnormal electrocardiogram, history of angina pectoris, evidence of renal

*Bistrium (hemamethonium bromide) was supplied by Casa Squibb, Lima, Peru, for study.

†In Cases 21 and 22 hypotension was unsuccessful; they are not included in the comparative study.

disease, severe complicated hypertension, and severe arteriosclerosis were not submitted to hypotensive anesthesia, but some of these conditions were present in the control group.

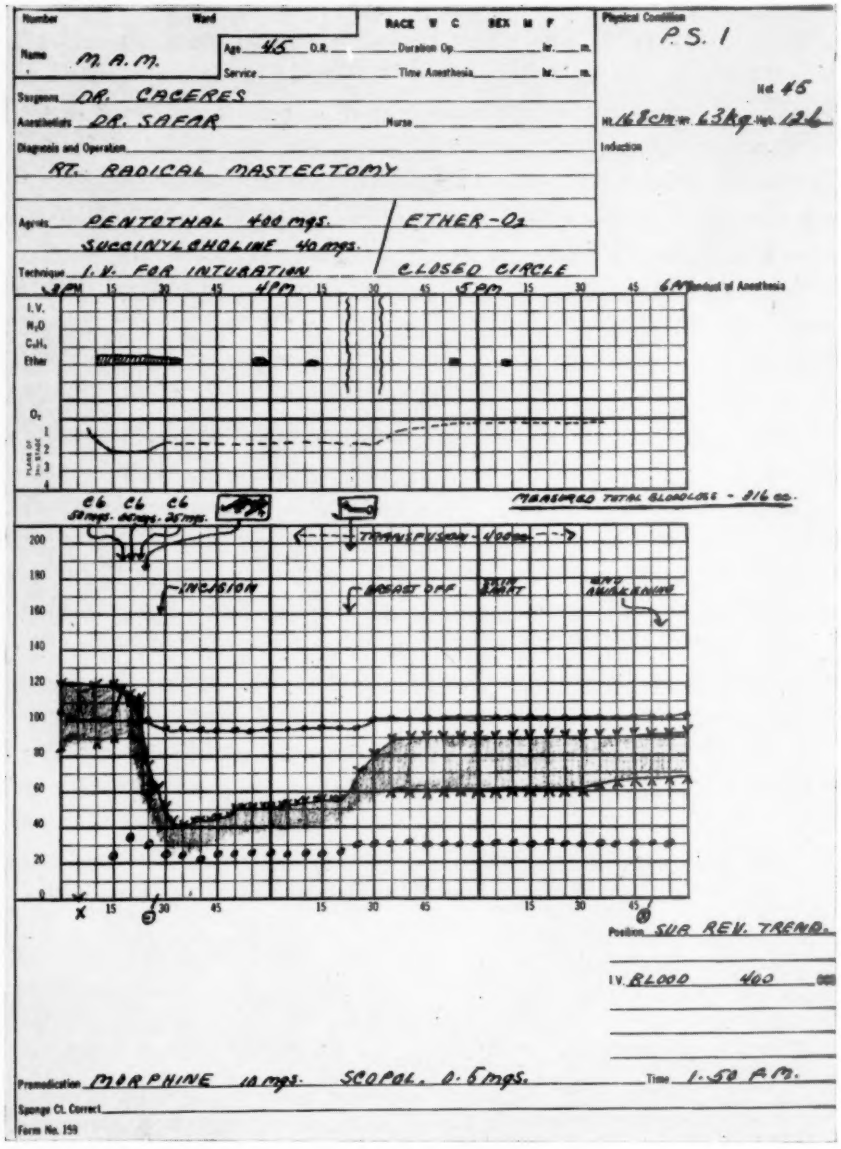

Fig. 1.—Record of a satisfactory hypotensive anesthesia.

TECHNIQUE OF HYPOTENSIVE ANESTHESIA

Fig. 1 represents a chart of a satisfactorily controlled hypotension.

Premedication.—All patients were premedicated individually with morphine, usually 10 mg., and scopolamine or atropine, usually 0.5 mg., one hour before anesthesia.

Anesthesia.—Induction and endotracheal intubation were performed with thiopental (200 to 500 mg.) and succinylcholine chloride (40 to 60 mg.). Im-

mediately after intubation, ether and oxygen were given by closed circle, the patient breathing spontaneously. Whenever the respirations appeared depressed they were assisted. All thoracotomies were performed under controlled respirations. Otherwise, spontaneous respirations were preferred since their alterations might serve as a warning sign of cerebral ischemia under hypotension and a sign of depth of anesthesia. The endotracheal airway was considered essential for the safety of this technique. Optimal oxygenation and absorption of CO_2 were stressed. N_2O was avoided to keep the oxygen concentration as high as possible. Cyclopropane was not used, as it may raise the blood pressure, except in the latter part of thoracotomies, when it was used while the blood pressure was allowed to rise.

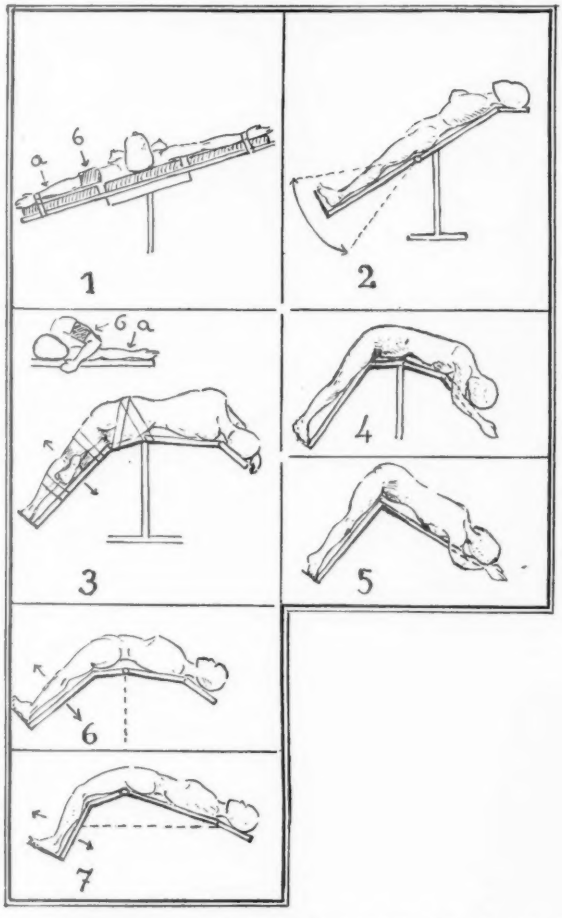

Fig. 2.—Positions for operations on breast (1 and 2), head and neck (2), thorax (3), back (4), perineum (5), upper abdomen (6), lower abdomen (7).

Hypotension.—When second plane of third-stage ether anesthesia was stabilized, 50 mg. of C_6 was injected intravenously slowly (over about thirty seconds). In previously hypertensive patients and those with very low body weight, only 25 mg. was injected. After this injection a finger remained continuously on the pulse. The blood pressure was checked every thirty seconds; if

TABLE I. SUMMARY OF FIFTY-THREE OPERATIONS PERFORMED UNDER CONTROLLED HYPOTENSION

	PT.	AGE (YR.), SEX	TYPE OF OPERATION	NORMAL BP (MM. HG)	C_6 TOTAL INDUCTION DOSE (MG.)	C_6 TOTAL MAINTENANCE DOSES (MG.)	LOWEST SYSTOLIC BP (MM. HG)	AVERAGE SYSTOLIC BP DURING RESECTION	HYPOTENSION BELOW 80 MM. HG (MIN.)	DURATION OF OPERATION (MIN.)	ASSISTANCE OF SURGERY BY ISCHEMIA (CLINICAL IMPRESSION)	TOTAL BLOOD LOSS (C.C.)	VASOPRESSOR USED AFTER HYPOTENSION	MAXIMUM CHANGE OF PULSE RATE AFTER C_6 (BEATS/MIN.)
1	AT	54F	Rad. mastectomy	160/90	100	0	45	63	90	145	Excellent	720	Yes	0
2	VD	40F	Rad. mastectomy	145/90	125	0	60	63	110	140	Good	620	No	+20
3	MA	45F	Rad. mastectomy	120/90	100	0	40	50	70	140	Excellent	316	No	+20
4	EA	42F	Rad. mastectomy	140/80	100	0	48	52	80	110	Good	516	No	+30
5	CA	52F	Rad. mastectomy	140/80	50	0	0	67	80	120	Good	502	Yes	0
6	DL	49F	Rad. mastectomy	140/90	62	0	40	59	75	140	Good	540	Yes	0
7	SA	28F	Rad. mastectomy	130/70	125	0	78	83	5	125	Some	566	No	+40
8	JA	46F	Rad. mastectomy	140/80	175	0	65	73	60	125	Excellent	322	Yes	+30
9	JY	38F	Rad. mastectomy	130/95	100	0	60	59	90	170	Good	378	No	+40
10	JV	56F	Rad. mastectomy	120/60	75	0	0	73	45	140	Excellent	342	Yes	+20
11	JC	37F	Rad. mastectomy	120/80	75	0	55	65	85	140	Excellent	706	No	+30
12	MA	51F	Rad. mastectomy	100/60	175	0	48	57	60	80	Excellent	202	No	+10
13	MU	61F	Rad. mastectomy	150/90	75	0	40	63	80	175	Excellent	212	Yes	+20
14	RL	28F	Rad. mastectomy	120/80	200	25	62	78	20	160	Excellent	290	No	+25
15	FF	33F	Rad. mastectomy	150/90	100	0	45	51	75	130	Excellent	162	No	+30
16	FS	54F	Rad. mastectomy	160/100	100	25	75	84	5	120	Excellent	280	Yes	0
17	LD	33F	Rad. mastectomy	110/80	75	0	60	66	70	150	Good	394	Yes	+40
18	JA	18F	Rad. mastectomy	100/70	50	0	50	66	80	200	Some or no	638	No	+25
19	CA	58F	Rad. mastectomy	150/90	50	0	50	69	140	240	Good	352	Yes	0
20	HV	47F	Rad. mastectomy	130/80	150	100	70	77	45	105	Good	372	No	+65
21	AV	39F	Rad. mastectomy	135/90	100	50	80	82	0	130	No	610	No	+70
22	ZS	28F	Rad. mastectomy	120/80	225	125	60	82	0	165	Some	990	No	0
23	CL	50M	Pneumonectomy (ca adhesions)	120/80	175	0	40	70	120	250	Excellent	548	No	+30
24	JB	46M	Pneumonectomy (ca invas. mediast.)	110/70	50	0	45	60	190	270	Excellent	788	No	+35
25	AF	53M	Pneumonectomy (ca)	140/100	100	25	60	68	115	300	Excellent	494	Yes	+70
26	JF	36F	Segm. resect, lung (hydatic cyst)	140/80	200	100	70	76	150	205	No	412	No	+40

27	RL	20F	Thoracotomy, res. 1 hydatic cyst	100/60	150	25	50	65	160	245	Excellent	402	No	+60
28	RM	50F	Thoracotomy, res. 1 hydatic cyst	130/80	100	0	55	65	125	225	Excellent	441	No	+20
29	TS	26F	Thoracotomy, res. 1 hydatic cyst	140/90	100	50	60	70	180	255	Good	425	No	+35
30	MF	23F	Thoracotomy, res. 1 hydatic cyst	110/70	125	50	70	74	125	240	Good	506	No	+80
31	MG	18F	Lobectomy (large hydatic cyst)	150/80	75	0	55	65	180	290	Excellent	279	No	+60
32	JG	16M	Thoracotomy, res. 18 hydatic cysts	110/70	150	0	50	76	120	435	Excellent	945	No	+30
33	CM	40M	Bilobectomy (large hyd. pulm. cyst)	120/70	75	0	60	70	150	350	Good	1,018	Yes	+60
34	LC	49F	Thoracot. extirp. huge neurofibro.	130/90	100	0	60	65	110	285	Good	2,761	No	+20
35	FP	54M	Thoracot. res. 2 pulm. abscesses	160/100	100	50	55	70	165	310	Excellent	520	Yes	+40
36	JZ	50M	Exc. ca face (maxilla; lip; nose)	140/90	125	0	80	102	0	200	No	484	No	+65
37	FS	55M	Exc. huge sarcoma face (maxilla)	130/80	50	150	70	86	10	170	Excellent	976	No	−10
38	GS	30F	Resection mandibula	110/70	100	75	48	60	100	190	Good	922	No	+40
39	LU	55F	Rhinoplasty	110/70	25	0	40	55	70	120	Excellent	96	No	+35
40	MR	22F	Exc. huge neurofibrosarcoma, back	110/60	100	0	52	62	90	135	Good	1,924	No	+25
41	IV	18F	Exc. lg. sarcoma of back	100/60	200	0	60	72	110	120	Good	348	No	+35
42	JS	48F	Radical mastectomy (atypical)	155/90	100	0	0	90	65	180	Good	992	No	+10
43	EV	38F	Simple mastectomy (atypical)	150/90	300	0	40	52	40	75	Excellent	382	No	+15
44	PR	53F	Craniotomy, exc. basal aneurysm	130/85	175	150	70	87	10	250	Good	—	No	+65
45	ZC	35F	Craniotomy, parietal, exc. glioma	115/80	100	25	40	63	75	200	Good ?	—	Yes	+20
46	FE	48M	Craniotomy frontal, exc. glioma	110/80	75	0	35	44	135	260	Some ?	—	Yes	+40
47	CA	50M	Craniotomy occip., exc., glioma	110/80	100	150	70	79	15	240	No ?	—	No	+25
48	GV	40M	Craniotomy, exc. cirsoid aneurysm	130/90	75	125	0	61	225	400	Good	—	No	+35
49	MB	40M	Laminect. lumb., exc. ependymoma	100/70	250	0	85	92	0	110	No	—	No	0
50	EA	58F	Craniotomy, exc. meningeoma	120/70	75	75	50	71	100	220	Excellent	—	Yes	−30
51	CM	25F	Lap. exc. large hydat. cyst, liver	100/90	75	25	65	74	40	200	Good	Ca 2,000	No	+15
52	DJ	36F	Rad. hysterectomy (Meigs)	120/80	150	200	70	89	20	350	Some ?	1,534	Yes	+30
53	ZI	39F	Pelvic evisceration (Brunschwig)	125/75	175	125	78	95	5	300	Good ?	Ca 1,000	No	+10

it was unchanged or raised two minutes after this first dose, another 25 mg. of C_6 was injected intravenously and another 25 mg. every two minutes until the slightest fall of blood pressure could be noted. At that moment the table was tilted into one of the positions demonstrated in Fig. 2 (for instance, for mastectomy into reverse Trendelenburg position of about fifteen to twenty degrees and turned lateral to elevate the side of operation). This change of posture usually dropped the blood pressure in the brachial artery considerably. The objective was a systolic blood pressure of between 50 and 70 mm. Hg. The incision was made only after the hypotension was induced and stabilized. The color of the arterial blood should be bright pink on incision, while the venous blood is usually very dark (slower blood flow, increased arteriovenous oxygen difference). The desired blood pressure level was controlled thereafter as much as possible only by increasing or decreasing the degree of tilt. To avoid change of the operative field, only the legs were moved occasionally after surgery was begun (Fig. 2).

If, within the first minutes after tilting, the blood pressure became unobtainable and/or the radial pulse disappeared, the degree of tilt was reduced. If necessary, the table was turned into Trendelenburg position and the intravenous fluids were speeded up. This usually was effective. If not, vasopressor drugs were used intravenously with caution; no more than 3 mg. of Vasoxyl, for instance, at a time. In the face of ganglionic blockade, vasopressors may cause excessive rise in blood pressure sometimes to dangerously high levels, which, by changing the circulatory balance, may do more harm than good.

When hypotension was accompanied by difficulty in measuring pressure by auscultation, measurements were made by palpation and oscillation. The blood pressure was not allowed to drop below 40 mm. Hg systolic. It is essential to obtain adequate hypotension from the initial dose of C_6. Within thirty minutes the blood pressure usually will begin to rise, and subsequent doses of C_6 are likely to be ineffective in lowering it again. In such instances intravenous morphine (5 mg.), d-tubocurarine, and controlled respirations in thoracic and abdominal operations were used at times to supplement the hypotensive effect of C_6 and posture.

Blood was replaced as it was lost. It was felt that a blood loss of more than 200 c.c. should not remain unreplaced under controlled hypotension. In anemic patients even more blood was given than was lost. When the resection was finished, the patient was restored to the horizontal or, if necessary, into slight Trendelenburg position. This action, in most instances, promptly raised the blood pressure to between 90 and 100 mm. Hg systolic. Only if the blood pressure did not stay above 90 was a pressor drug employed cautiously, avoiding an excessive overshooting effect. Intramuscular doses of 10 mg. of Vasoxyl or Methedrine were preferred over intravenous drip techniques. The latter may cause a more abrupt hypertension, which may present, postoperatively, a considerable burden for the nursing personnel. In previously hypertensive patients the postoperative objective was a blood pressure above 100-110 mm. Hg systolic.

Horizontal or slight Trendelenburg position was maintained during the postoperative period until diuresis started, the blood pressure became stabilized, and mydriasis and pupillary paralysis disappeared (all signs of cessation of ganglionic blockade).

DATA

Failure to produce hypotension below 80 mm. Hg systolic for a sufficient period of time was seen in eight operations (Nos. 7, 21, 22, 36, 37, 44, 49, 53 of Table I). In the others the blood pressure was lowered satisfactorily. The essential data of all fifty-three operations are summarized in Table I, those of the operations used for the controlled study in Tables II and III.

TABLE II. DATA ON FORTY TYPICAL RADICAL MASTECTOMIES PERFORMED WITH AND WITHOUT HYPOTENSIVE ANESTHESIA

	20 MASTECTOMIES HYPOTENSIVE ANESTHESIA			20 MASTECTOMIES NORMAL ANESTHESIA		
	MIN.	MAX.	AVG.	MIN.	MAX.	AVG.
1. Surgical blood loss (measured) (c.c.)	162	720	421	773	1,316	883
2. Duration of operation (min.)	80	240	143	120	255	169
3. Duration of resective part of operation (min.)	40	90	67	60	140	90
4. Total number of clamps used for hemostasis	110	166	134	198	235	222
5. Excessive hemorrhagic wound drainage postop. (no. of cases)			1			2
6. Severe postop. hemorrhage (no. of cases)			0			1
7. Thrombophlebitis postop. (no. of cases)			0			1
8. Slight pulmonary complication postop. (no. of cases)			1			1

TABLE III. MEASURED SURGICAL BLOOD LOSS OF TYPICAL OPERATIONS

TYPE OF OPERATION	SATISFACTORY HYPOTENSIVE ANESTHESIA				NORMAL ANESTHESIA			
	NO. OF CASES	TOTAL BLOOD LOSS (C.C.)			NO. OF CASES	TOTAL BLOOD LOSS (C.C.)		
		MIN.	MAX.	AVG.		MIN.	MAX.	AVG.
1. Radical mastectomy	20	162	720	421	20	773	1,316	883
2. Thoracotomy—incision alone	13	24	340	135	12	32	266	172
3. Extirpation of one pulmonary cyst (Echinococcus)	5	402	506	437	6	490	1,226	721
4. Pneumonectomy (carcinoma)	3	494	788	610	2	1,300	1,890	1,595
5. Lobectomy	1	–	–	279	2	881	934	907
6. Operation no. 27—bilateral resection of pulmonary cyst (Echinococcus), 1 cyst each side, approximately same size	1	same patient						
		rt. side total		402		lft. side total		1,226
		rt. incision		194		lft. incision		246
7. Operation no. 32—bilateral resection of multiple pulmonary cysts (Echinococcus)	1	same patient						
		rt. side (18 cysts)				lft. side (6 cysts)		
		total		945		total		684
		rt. incision		130		lft. incision		196

Blood Loss and Facilitation of Surgery.—The total blood loss was lower in all cases of satisfactory hypotension (below 80), as compared with normotensive anesthesias, but a completely dry field was never seen, even with a systolic blood pressure as low as 40 mm. Hg. The reduction of blood loss was not always related to the degree of hypotension (Fig. 3). Case No. 18 is an example of considerable bleeding with a blood pressure of 60, and in Case No. 16 ischemia

seemed excellent with a blood pressure around 80. In general, if in previously normotensive persons the systolic blood pressure was lowered only to 80 or 90 mm. Hg the small vessels sometimes oozed diffusely, even in the elevated area. This did not facilitate hemostasis and dissection even though the total blood loss was reduced. It is felt, therefore, that in previously normotensive individuals, blood pressure levels of between 45 and 65 mm. Hg are necessary to assist surgery significantly. In previously hypertensive patients, surgery may be assisted with a blood pressure of about 80 mm. Hg. Whenever the operative site could not be elevated, ischemia was not impressive (abdominal surgery).

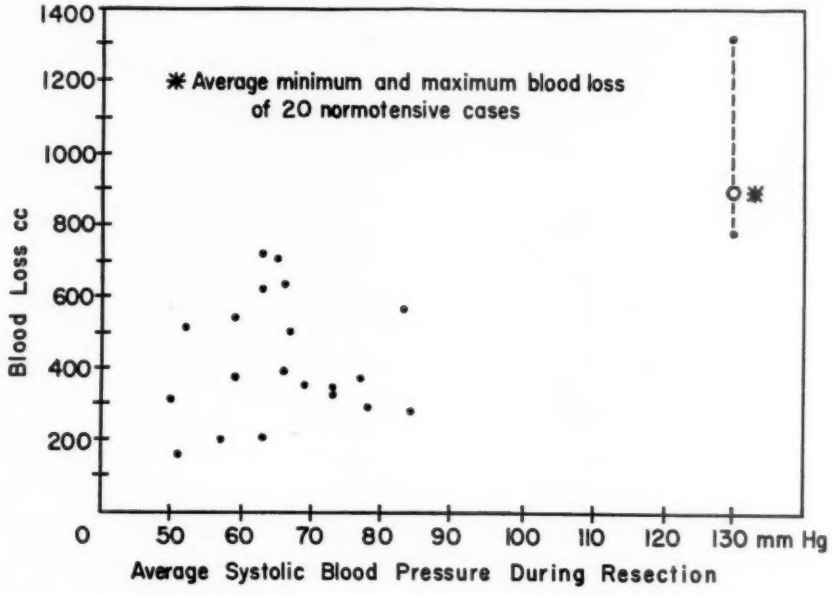

Fig. 3.—Relationship between blood loss and degree of hypotension in radical mastectomies.

In *radical mastectomies* under controlled hypotension (Table II) the bleeding points could be clamped more easily since with slower bleeding they were more readily seen. Fewer clamps were used. The time required for resection was shorter. The total operating time was reduced by an average of twenty-six minutes. The blood loss, which ranged from 162 c.c. to 720 c.c., was smaller in all hypotensive cases than in the driest normotensive one. Eight of the twenty patients lost more than 500 c.c. The difference in blood loss between the hypotensive and normotensive groups averaged 462 c.c. Blood transfusion was considered necessary in all patients but one of the hypotensive group (No. 15).

In all *intrathoracic operations* the total blood loss was considerably reduced (Table III), particularly in the more extensive resections, by the use of controlled hypotension. Bleeding from incision of the chest wall varied greatly in both groups, from 24 to 340 c.c. in the hypotensive group, from 32 to 266 c.c. in the normotensive group. The dissection of pleural adhesions and particularly of the structures about the hilus was always much facilitated by hypotension. There was less oozing from interstitial tissues. The large vessels in the hilus (pulmonary vein and artery) were soft and more easily separable. This observa-

tion is in agreement with the lower pulmonary artery pressures measured under similar conditions in man.[14] No operation in either group produced any significant reflex circulatory disturbance.

The data on two patients with bilateral thoracotomies for multiple hydatid cysts of both lungs are seen in Table III. These patients served as their own controls, one side being performed under normal anesthesia, the other under controlled hypotension.

In *neurosurgery* our experience was limited to seven patients. Bleeding from the venous sinuses, a not uncommon surgical complication, appeared unchanged even with an arterial blood pressure of 40 mm. Hg. Central venous pressure has been found by others to be unchanged under this technique.[15] The resection of brain tumors was definitely facilitated as long as only small vessels were involved. Profuse arterial bleeding from the intracranial carotid artery during resection of a cirsoid aneurysm (No. 48) with blood pressures of between 40 and 60 mm. Hg could be controlled only by compression and ligation of the common carotid artery at the neck. Cardiac action became very poor with arrest, perhaps imminent on two occasions, since pressure transfusions could not keep up with the rate of blood loss.

In the three radical *abdominal operations* (Nos. 51, 52, 53) ischemia seemed fair as long as large vessels were not injured. The pelvic veins bled profusely. The liver tissue on excision of an enormous Echinococcus cyst of the liver (No. 51) bled less after hypotension was induced during the operation. The surgeon had considered this cyst as not resectable. Hypotension enabled surgical resection and cure from a lesion which otherwise, if only drained, results in morbidity of months or years.

The *extensive tumor surgery* in Cases Nos. 34, 37, 40, 41 was performed with great rapidity, and it was felt that blood was saved by having chosen deliberate hypotension. The lesion in Patient No. 37 was made resectable only by the choice of this technique.

Observations Concerning the Management of Hypotensive Anesthesia.—Usually less *anesthetic agent* was required for the patients under controlled hypotension.

The *blood pressure* and radial pulse became unobtainable in three cases in the absence of hemorrhage, soon after the induction dose of C_6 was given (Nos. 5, 10, 42), while respirations, patient's color, skin temperature, and capillary refill time remained unchanged and the temporal pulse remained palpable. The blood pressure recovered in all these instances immediately after the legs were raised.

A single injection of C_6 produced some blood pressure response within two minutes after intravenous injection. The maximal hypotension was evident about five to seven minutes after injection. Several doses injected within two-minute intervals seemed to be additive, without producing the tachyphylaxis, which was seen after repeated injections later.

The first injection of C_6 in four cases (Nos. 20, 23, 25, 31) was followed by an initial rise of the blood pressure within two to four minutes after injection, hypotension coming on thereafter following the positioning of the patient and the adding of subsequent doses of C_6.

In about one-half our patients in whom the blood presure was easily lowered with C_6, the pentothal induction dose had failed to produce such an effect. The hypotensive effect of pentothal might have escaped our attention at times, because of the blood pressure rise from endotracheal intubation and succinylcholine.

The *heart rate* increased within thirty seconds after injection of the first dose of C_6 in forty-four of the fifty-three cases (83 per cent), remained unchanged in seven, and was slowed in two. In fifteen cases the heart rate increased by more than 40 beats per minute, in one by 80 beats per minute. The peak tachycardia occurred always immediately and leveled off thereafter spontaneously in all cases usually to a rate between 100 and 120. This tachycardia occurred even when the blood pressure remained unchanged. It was not reproduced or increased by subsequent doses of C_6.

Twenty to thirty seconds after injection of the first dose of C_6 we observed occasionally one to two deep breaths followed by a short period of irregular *respirations,* whether or not the blood pressure was unchanged. This was sometimes observed also after subsequent doses.

The *pupils* started dilating about sixty seconds after the first injection, and either maximal mydriasis developed within the following five minutes, or slight mydriasis was increased by subsequent doses. Postoperatively the mydriasis and pupillary paralysis disappeared gradually within six to twelve hours. The degree of mydriasis was not necessarily related to the degree of hypotension.

Postoperative recovery of consciousness was slightly slower in the hypotensive groups, although usually the patients reacted and obeyed simple orders at the end of operation. No clinically impressive difference in postoperative pain and restlessness was observed in either group of patients. Most patients showed slight hypothermia at the end of operation. The lowest temperature observed was in Patient No. 12, who had a temperature of 35° C. (95° F.) for several hours.

Diuresis started promptly in all but two instances as soon as the blood pressure recovered above 80 mm. Hg systolic and the patient became conscious. It also occurred after hypotension of between 40 and 50 mm. Hg systolic for two hours or more. Amount and onset of diuresis were in no relation to the degree of hypotension during operation or to the dose of C_6 injected. Patients under the influence of C_6 with systolic blood pressures above 90 mm. Hg seemed to produce more urine in the early postoperative hours than those after normal anesthesia. This statement is based only on routine input/output records.

Postoperative Complications.—There were two deaths in this series: One postoperative reactive hemorrhage after what appeared to be adequate hemostasis (No. 35); one uncontrollable postoperative hemorrhage after inadequate hemostasis (surgical error) (No. 52).

One bronchopneumonia, mild, was controlled within two days. Two prolonged postoperative hypotensions occurred (twenty-four and seventy-two hours), probably explained by poor urinary output and slow elimination of C_6. Both patients had an otherwise uneventful recovery.

In forty-eight operations the recovery from anesthesia was uncomplicated. Rough clinical follow-up after operation revealed no organic damage which could be attributed to the anesthetic technique, but function tests of vital organs were not performed as a routine.

DISCUSSION

Spinal anesthesia was not chosen for the production of vasoparalysis for the following reasons: It would have to be combined with general endotracheal anesthesia for operations on the upper half of the body and this would have made the technique more complicated. Theoretically, spinal anesthesia produces a less complete sympathetic block[16] and no interruption of certain parasympathetic impulses, while ganglionic blocking agents are supposed to block both parts of the autonomic nervous system, causing "stabilization."

It is surprising how frequently blood pressure is maintained at normal levels in the face of either spinal anesthesia or ganglionic blocking agents. In resistant cases, morphine or d-tubocurarine seems a more logical supplementation of C_6 than a relative overdose of the anesthetic agent or controlled respirations. The latter factors reduce the blood pressure not only by vasoparalysis but by direct depression of the myocardium and reduction of venous return to the heart, which may lead unexpectedly to cardiac arrest. A later case in my experience demonstrated such a complication. If pooling of blood into the lower extremities by posture alone is unsuccessful, suction applied to the legs, which has been recommended by others,[17] may be used.

Moment-to-moment observation of the vital signs is essential to detect warning signs of cerebral and coronary ischemia. Sudden cardiac arrest may follow if the blood pressure is not raised immediately. This is illustrated by an episode in Patient No. 13: After fifteen minutes of hypotension of 50, the pulse became slow and irregular, respirations fast, deep, and gasping, and the patient was sweating profusely, while the pupils were only moderately dilated. These latter signs made us believe that ganglionic block was incomplete. Turning the patient into horizontal position raised the blood pressure immediately to 70 and all these signs disappeared.

The response to a single dose of C_6 varied greatly from patient to patient. Hypertensive, old, and arteriosclerotic individuals are much more sensitive than young normotensive ones. Two extremes in our experience demonstrate this: One severe hypertensive patient (not in this series) received (during an abdominal operation under cyclopropane-ether anesthesia), because of progressive rise of the blood pressure, 6 mg. C_6 intravenously which dropped the systolic blood pressure from 210 to 80 mm. Hg without change of position. Other patients (Table I) received more than 200 mg. of C_6 without significant hypotensive response. Because of this unpredictable response, and to avoid an excessive first dose, we have induced hypotension by "titration," as described

previously. The table was not tilted at the very moment of injection of C_6 since disappearance of the pulse was occasionally observed. Venous return to the heart was probably too suddenly reduced. Nor was the table tilted before the injection of C_6 because we had the impression that occasionally induction of hypotension was more difficult then, perhaps because compensatory vasomotor tone was provoked by the change of posture.

The degrees of mydriasis and paralysis of the pupils seem to be fairly reliable indications of the blood concentration of C_6.

The occasional initial hypertension, tachycardia, and respiratory changes seen after the injection of C_6 may theoretically be explained by a hyperactive carotid sinus reflex, initiated by a slight momentary hypotension from the first dose, while the ganglionic block is still incomplete.

It is often difficult to decide whether hypotensive anesthesia is justified before the exploratory part of surgery has been accomplished. We believe it is safe to induce hypotension at that time (Cases Nos. 39, 51) if the surgeon stops working until the low blood pressure is stabilized. If possible, the ganglionic blocking agent should certainly not be given during active hemorrhage.

The two *deaths* in this series occurred postoperatively. One was due to employment of the hypotensive technique (No. 35): after an uneventful thoracic operation the chest wall was closed with what appeared to be adequate hemostasis, with a blood pressure of 90 mm. Hg systolic; since the blood pressure did not rise higher during closure, two doses of 10 mg. Vasoxyl each were given intramuscularly. Fifty minutes after the end of operation, cardiac arrest occurred, and when the chest was opened, about 2,000 c.c. of blood was found in the pleural cavity and the heart was empty and in maximal systole. The bleeding came from the chest wall. The clinical signs of shock were altered by C_6. Peripheral vasoconstriction, sweat, and pallor were absent and the progressive drop of blood pressure not detected in time because of these factors and incompetent attention. The drainage tube from the chest had remained clamped by mistake. It is felt this patient could have been saved by immediate thoracotomy if the bleeding had been recognized in time. The Vasoxyl given after hemostasis could have been a causative factor in this reactive hemorrhage. There is evidence that rapid massive hemorrhage and/or asphyxia,[21] to a degree which the normal organism survives, can lead, under C_6 hypotension, to death from rapid collapse of circulation and respiration. This is probably due to the blockade of the sympathoadrenal protective mechanism.[21] This was demonstrated also by two other cases of hemorrhage from large vessels (Nos. 48, 52). On the other hand, there is some evidence that autonomic blockade may protect against shock from trauma or hemorrhage.[22] This still remains to be proved. In general, a blood pressure of 90 to 100 mm. Hg in a previously normotensive person seems adequate to show all bleeding points and permit meticulous hemostasis. Theoretically, during recovery from vasoparalysis a gradual rise of the blood pressure will be accompanied by an increase of vasomotor tone; the vessel wall will clamp down on the clot, avoiding its ejection. Nevertheless, reactive hemorrhage is an ever-present possibility with this technique.[23, 24]

The second death in this series was entirely due to surgical error (No. 52). The abdomen was closed without control of diffuse bleeding from pelvic vessels.

The *hazards* of this technique are many: sudden cardiac arrest appears to be the greatest danger.[23] It can be explained by blood volume deficit, pooling of blood into veins (loss of venomotor tone),[25] and/or deficient coronary blood flow. With controlled hypotension the contractile force of the heart seems reduced[21] and cardiac output is diminished.[14, 25] There are few data available on blood flow through vital organs during hypotensive anesthesia. Although skin blood flow seems to be adequate, blood flow through a vital organ whose vascular bed is already damaged may be insufficient. There are observations of myocardial infarction,[23, 24, 26] liver damage,[24, 27, 28] brain damage, including blindness,[23, 24, 28, 29] and reduced renal blood flow.[28, 30] We have not seen obvious organic damage after systolic blood pressure levels of between 50 and 60 mm. Hg for two to three hours and more. This report demonstrates that the majority of patients can survive, but does not reduce the hazard demonstrated by a fair number of accidents.

The perfusion pressure of the *brain* in reverse Trendelenburg position is lower than arterial blood pressure measured at heart level on the arm, due to the hydrostatic effect.[9]

The cerebral blood flow falls significantly with reduction of mean arterial pressure.[31] Figures obtained from Finnerty and associates[31] show that the critical level of cerebral blood flow, below which clinical signs of cerebral ischemia occur (hypotension produced by C_6 and posture in unanesthetized subjects), is fairly constant (average 31.5 c.c. per 100 grams of brain per minute). The arterial hypotension which leads to this critical level, however, varies greatly: from about 30 mm. Hg mean arterial pressure (at brain level) in previously normotensive persons to about 90 mm. Hg in previously hypertensive persons.[31]

In analyzing the data on *blood loss* it is recognized that the amount of hemorrhage varied a great deal from patient to patient under normal anesthesia in standard operations. These differences cannot be entirely explained by differences of body constitution, blood pressure, or type of anesthesia. An important factor related to blood loss is the vascular status of the tissue involved. An instance of this may be the hormonal status of the patient undergoing a breast operation.

Although the reduction of blood loss by hypotensive anesthesia in our mastectomy group may appear of significance, actually it is of minor value to the patient. Under normal anesthesia it is perfectly safe to transfuse only 500 c.c. of blood when 800 c.c. was lost. Under controlled hypotension all our patients but one had to be transfused anyway.

The same argument can be made about the other standardized operations in our series. The shortening of anesthesia time by thirty minutes in an operation which lasts from two to four hours is little gain in the presence of modern normotensive anesthesia, which, in the good risk patients, can be prolonged for several hours without additional harm to the patient. At the end of a prolonged normotensive anesthesia, the status quo with all protective reflexes recovered will

be obtained sooner than after hypotensive anesthesia. The extensive use of this method in a busy operating schedule puts a great additional strain on the anesthesia and nursing teams.

It is remarkable that thoracic surgery is assisted considerably in spite of its "central" site, without taking advantage of the posture. However, clean, technically simple resections in the thorax can also be dry with normal technique, and the amount of blood which might be saved is insignificant (Table III). In extrapleural pneumonectomies the hypotensive technique might be of value.

Of our fifty-three patients, only two had "absolute indications" for the choice of deliberate hypotension (Nos. 37, 51). Three others (Nos. 34, 40, 41), although considered operable under normal anesthesia, represent "relative indications," because of the considerable facilitation of dissection, permitting cleaner and more radical tumor surgery, and, perhaps, the reduction of blood transfused. The assistance to the surgeon in difficult dissections cannot be neglected. This factor should not make us choose hypotensive anesthesia. It has been shown that serious complications associated with hypotensive anesthesia are directly related to the degree of the reduction of the blood pressure from the preoperative level.[24] Most of the accidents in healthy persons undergoing harmless operations probably never appeared in the literature.[23, 24, 28]

We have also used, in patients who are not included in this study, Arfonad,* a thiophanium derivative, as the ganglionic blocking agent.[18] When the patient is sensitive to its injection in small amounts, Arfonad seems to be more rapidly destroyed than is C_6. At the end of the operation the pupils are usually small and the blood pressure stable and normotensive, which makes postoperative care easier. Because of its short action it is best given by intravenous drip (1 mg. per cubic centimeter), which produces a more controllable hypotension than C_6.[19, 20] At times it was difficult to produce a smooth hypotension with Arfonad because of the variability of the intravenous drip.

SUMMARY AND CONCLUSIONS

The data obtained from forty standard operative procedures (radical mastectomy), performed under either normotensive or hypotensive anesthesia under fairly controlled conditions, and the observations made on other operations performed under hypotensive anesthesia, including measurement of surgical blood loss, are reported.

The technique chosen for deliberate hypotension was the combination of hexamethonium bromide and change of posture. An attempt has been made to define the degree of assistance to patient and surgeon offered by this method.

The following conclusions were drawn from these data:

1. Standard operations which can safely be performed under normal anesthesia without excessive hemorrhage are no indication for the selection of deliberate hypotension. The total blood loss (measured) is reduced, but not to an extent that transfusions are made unnecessary. The operative time is

*Arfonad was given to us by Hoffmann-La Roche, Inc., Nutley, New Jersey, for investigation.

reduced but not significantly. The only gain from the choice of this technique, in this group, was the facilitation of surgical dissection. This alone should not justify its use.

2. The rare lesion which is inoperable under normal anesthesia because of the likelihood of uncontrollable hemorrhage represents an absolute indication for the choice of this method (only two of the fifty-three cases in this series).

If rapid blood loss from large arteries or veins is to be expected, deliberate hypotension should not be selected. Venous bleeding is practically unaltered by this technique.

3. If, in extensive resective surgery, excessive bleeding is to be expected. both surgeon and patient may be assisted by hypotensive anesthesia, if only small vessels are involved, if the operative site can be placed uppermost, and if the proper patient is selected. The major problem in selecting this technique today is our inability to be certain in which patient hypotension may reduce blood flow to a vital organ below its essential level. The relative safety of this technique is only possible when close cooperation between surgeon and anesthesiologist exists.

4. In selected patients excessively large numbers of transfusions, which occasionally can lead to uncontrollable oozing, may be avoided by controlled hypotension.

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REFERENCES

1. Phemister, D. B., Laester, C. H., Eichelberger, L., and Schachter, R. J.: Afferent Vasodepressor Nerve Impulses as a Cause of Shock. Tested Experimentally by Aortic Depressor Nerve Stimulation, Ann. Surg. **119**: 26, 1944.
2. Dale, H. H., and Laidlow, P. P.: Histamine Shock, J. Physiol. **52**: 355, 1919.
3. Blalock, A.: Shock, Surg., Gynec. & Obst. **64**: 245, 1937.
4. Gardner, W. J.: The Control of Bleeding During Operation by Induced Hypotension, J. A. M. A. **132**: 572, 1946.
5. Enderby, G. E. H.: Controlled Circulation With Hypotensive Drugs and Posture to Reduce Bleeding in Surgery. Preliminary Results With Pentamethonium Iodide, Lancet (London), **1**: 1145, 1950.
6. Enderby, G. E. H., and Pelmore, J. F.: Controlled Hypotension and Postural Ischemia to Reduce Bleeding in Surgery; Report of 250 Cases, Lancet (London) **1**: 663, 1951.
7. Enderby, G. E. H.: Postural Ischemia and the Use of the Methonium Compounds, Current Res. in Anesth. & Analg. **32**: 1, 1953.
8. Enderby, G. E. H., Davison, M. H. A., Korkis, F. B., Barnes, M., and others: Discussion of the Use of Hypotensive Drugs in Surgery, Proc. Roy. Soc. Med. (London) **44**: 829, 1951.
9. Enderby, G. E. H.: Postural Ischemia and Bloodpressure, Lancet (London) **1**: 185, 1954.
10. Griffiths, H. W. C., and Gillies, J.: Thoraco-lumbar Splanchnicectomy and Sympathectomy. Anesthetic Procedure, Anesthesia **3**: 134, 1948.
11. Gillies, J.: Anesthetic Factors in Causation and Prevention of Excessive Bleeding During Surgical Operations. Joseph Clover Lecture, Ann. Roy. Coll. Surgeons England **7**: 204: 1950.
12. Wangensteen, O. H.: The Controlled Administration of Fluids to Surgical Patients Including Description of Gravimetric Methods of Determining Status of Hydration and Blood Loss During Operation, Minnesota Med. **25**: 783, 1942.
13. Safar, P., and Caceres, E.: Perdida sanguinea durante las operaciones quirurgicas, Ann. Faculdad Medicina (Lima) **36**: 171, 1953.
14. Gilmore, H. R., Kopelman, H., McMichael, J., and Milne, I. G.: Effect of Hexamethonium Bromide on the Cardiac Output and Pulmonary Circulation, Lancet (London) **2**: 898, 1952.

15. Boyan, C. P., and Brunschwig, A.: Hypotensive Anesthesia in Radical Pelvic and Abdominal Surgery, SURGERY **31**: 829, 1952.
16. Brust, A. A., Reiser, M. F., and Ferris, E. B.: Evaluation of Neurogenic Control of Blood Pressure in Hypertension With Tetraethylammonium Chloride and Spinal Anesthesia, J. Clin. Invest. **30**: 925, 1951.
17. Saunders, J. W.: Negative-Pressure Device for Controlled Hypotension During Surgical Operations, Lancet (London) **1**: 1286, 1952.
18. Randall, L. O., Peterson, W. G., and Lehman, G.: The Ganglionic Blocking Action of Thiophanium Derivatives, J. Pharmacol. & Exper. Therap. **97**: 48, 1949.
19. Magill, F. W., Scurr, C. F., and Wyman, J. B.: Controlled Hypotension by a Thiophanium Derivative, Lancet (London) **1**: 219, 1953.
20. Nicholson, M. J., Sarnoff, S. J., and Crehan, J. P.: The Intravenous Use of a Thiophanium Derivative (Arfonad-Ro 2-222) for the Production of a Flexible and Rapidly Reversible Hypotension During Surgery, Anesthesiology **14**: 215, 1953.
21. Cotten, M. deV., Brown, J. M., and Kronen, P. S.: Heart Force Responses to Pressor Amines During Hypotension Produced by Hexamethonium, Anesthesiology **15**: 126, 1954.
22. Wyman, J. B.: Discussion on Hypotension During Anesthesia, Proc. Roy. Soc. Med. **46**: 605, 1953.
23. Editorial: Warning, Anesthesia (London) **7**: 65, 1952.
24. Hampton, L. J., and Little, D. M., Jr.: The Results of a Questionnaire Concerning the Use of Controlled Hypotension in Anesthesia, Lancet (London) **1**: 1299, 1953.
25. Shackman, R., Graber, I. G., Melrose, D. G., and Smith, J.: Hemodynamics of Methonium Hypotension During Anesthesia, Anaesthesia (London) **7**: 217, 1952.
26. Zukschwerdt, L., discussion of Kern, E.: Blutdrucksverminderung durch Kontrollierte Herbsetzung des Blutdruckes, Anaesthesist **1**: 26, 1952.
27. Feuerstein, V., discussion of Kucher, R., and Steinbereithner, K.: Klinische Erfahrungen mit der Ganglienblockade, Anaesthesist **1**: 156, 1952.
28. Leading Article: Complications of Controlled Hypotension, Lancet (London) **2**: 25, 1952.
29. Wirtinger, W.: Erfahrungen mit der Kuenstlichen Blutdrucksenkung in der operativen Hals-Nasen-Ohrenheilkunde, Anaesthesist **2**: 85, 1953.
30. Mackinnon, J.: Effect of Hypotension-Producing Drugs on the Renal Circulation, Lancet (London) **2**: 12, 1952.
31. Finnerty, F. A., Wilkin, L., and Fazekas, J. F.: Cerebral Hemodynamics During Cerebral Ischemia Induced by Acute Hypotension, J. Clin. Invest., 1954. In press.

Appraisal of Progress in Surgical Therapy

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THE PROBLEM OF THE BLEEDING PEPTIC ULCER

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THE nature of the treatment of patients bleeding from peptic ulcer is controversial because there are many facets to be considered. Each of these may assume a dominant role at one time or another and within the same course of the same patient. Thus a factor likely to account for the death of a patient may play an irrelevant role in another; and for that matter it may be an unimportant consideration later on in the same patient with an episode of recurrence of bleeding. The controversy as to choice of treatment is largely resolved when the physician considers the needs of the individual patient and how they can best be met within the confines of his medical community. This involves the choice of the proper treatment for the appropriate patient at the right time.

This presentation is a summary of principles as stated by many and confirmed by personal experience.

CAUSE OF DEATH FROM THE BLEEDING PEPTIC ULCER

Reported experience as to the cause of death during an episode of bleeding from peptic ulcer varies considerably with the result that these are better listed than assigned an order of frequency. Among the causes encountered is exsanguinary hemorrhage in which death occurs before or shortly after medical aid becomes available. Death from bronchopneumonia, which in our experience nearly always results from aspiration at the time of massive hematemesis, is fatal in most instances in spite of a prompt bronchoscopic toilet. Renal failure from prolonged shock, often complicated by the consequences of a mismatched blood transfusion, remains among the ravages of haste so common to this disease.

If there is one cause of death that exceeds the others, it is the intractable bronchopneumonia from gastric aspiration. There remain secondary causes of death which are limited principally to cardiovascular accidents and pulmonary embolism. These more often are seen in the older age group when death occurs.

PATHOLOGY OF THE BLEEDING ULCER

The massively bleeding gastric or duodenal ulcer lies in an area where it erodes a major artery. The artery or branches usually involved are the left

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gastric in the case of the gastric ulcer and the gastroduodenal when the duodenal ulcer is the source of bleeding. Rarely the splenic artery is eroded by a gastric ulcer and even less often the aorta itself; in both instances fatality is the rule.

In any case, there is one feature of the pathologic anatomy in the patient with the massively bleeding ulcer which is common to all who suffer massive bleeding. It is the posterior location of the ulcer. The posterior ulcer penetrates but seldom perforates into the free peritoneal cavity. For the same reason, a perforating ulcer is seldom the site of massive hemorrhage. Its location is generally the anterior surface of the stomach or duodenum where it can communicate with the free peritoneal cavity. The anterior surfaces of both the duodenum and the stomach contain no major arteries; the vessels lying anteriorly are small by comparison with those found on or in the posterior regions (Fig. 1). For the most part the occurrence of perforation excludes the probabilitiy of a massive hemorrhage just as often as the massively bleeding ulcer rarely perforates.

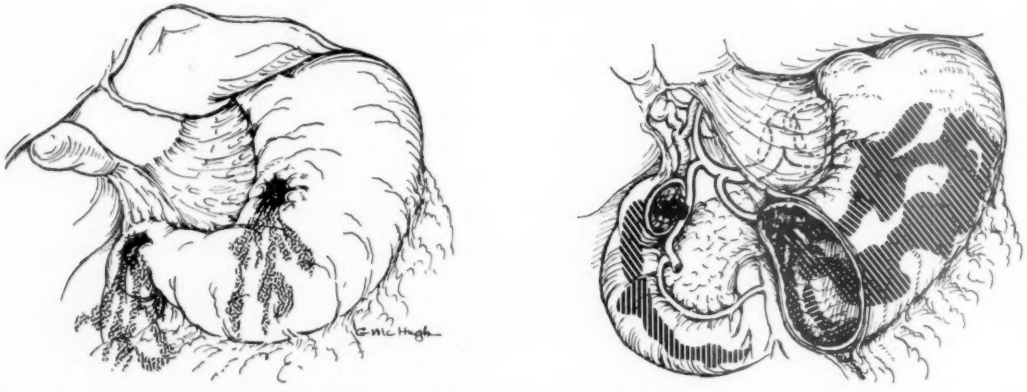

Fig. 1.—Artist's illustration demonstrating the anatomic reasons why the perforating peptic ulcer which usually lies on the relatively nonvascular anterior portion of the stomach or duodenum seldom gives rise to massive hemorrhage. The peptic ulcer which bleeds massively is usually located posteriorly in the regions of the major vessels. The posterior ulcer is seldom able to perforate into the free peritoneal cavity.

There are certain pathologic considerations which favor continued bleeding or its intermittent but frequent and prompt recurrence. These are pathologic features which tend to interfere with the normally expected constriction of the eroded artery. The arteriosclerotic nature of vessels among the aged favors its patency and continued bleeding. Occasionally, such an artery projects above the ulcer bed, and it is difficult if not impossible to effect prompt healing about it. The patient suffering from a chronic ulcer is also likely to bleed continuously or to have an early recurrence. Such bleeding arteries are frequently thickened and enmeshed within the scar (Fig. 2). This state of affairs more often is observed among the older patient and adds to his pre-existing problem of arteriosclerosis.

Finally, there remain those patients, some 15 to 20 per cent, whose massive bleeding from the stomach or duodenum is due to causes other than peptic

Fig. 2.—Photomicrograph demonstrating the thickened arterial walls enmeshed in the ulcer bed of the stomach of a 40-year-old man whose ulcer history dated eight years at the time of resection. There is mechanical interference with constriction of these vessels by the fibrous tissue in the vessel walls as well as within the ulcer bed.

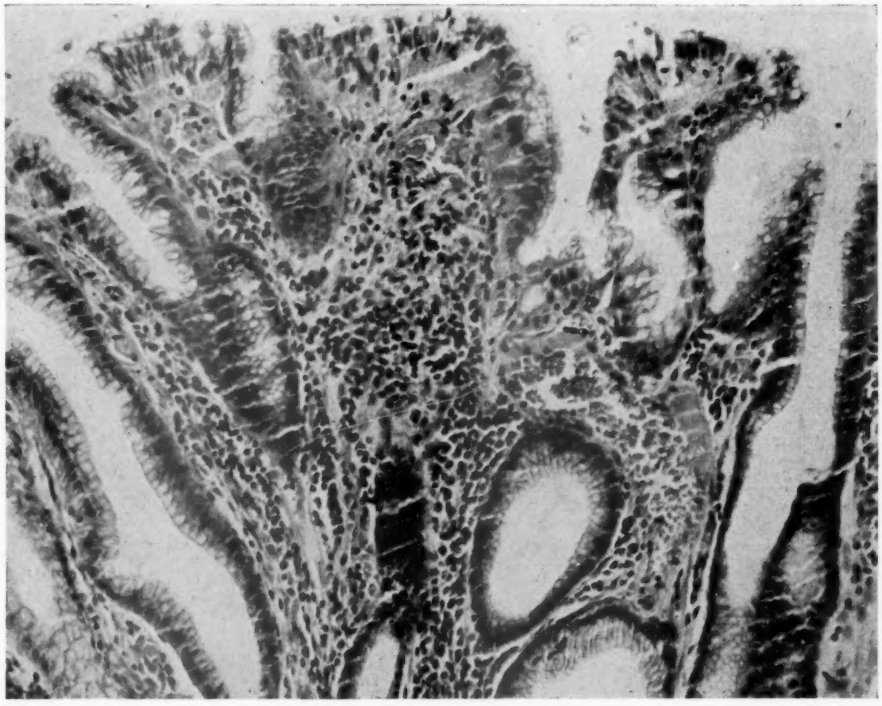

Fig. 3.—Photomicrograph showing numerous small vessels within the submucosal area which collectively accounted for gastrostaxis requiring subtotal gastric resection.

ulcer. The cause most likely to be overlooked and to lead to abandonment of resection is the patient suffering from "Gastrostaxis." For the most part these are patients with gastritis: atrophic, hypertrophic, or acute erosive gastritis. Illustrating the impossibility to detect a bleeding lesion grossly is the photomicrograph in Fig. 3, in which the unrelenting serious gastric hemorrhage appeared the result of a venous telangiectasia. A subtotal gastrectomy brought the desired relief from hemorrhage.

SYMPTOMS AND DIAGNOSIS

Massive bleeding from peptic ulcer is a self-evident symptom. Although most agree that approximately 85 per cent of all patients who exhibit this symptom suffer from a peptic ulcer, its origin is sufficiently obscure at times as to embarrass the surgeon occasionally in his search for the bleeding point. Esophageal and gastric varices account for 5 to 10 per cent of patients with massive hemorrhage. Gastritis, esophagitis, venous telangiectasia of the gastric mucosa, benign and malignant tumors, blood dyscrasias, and other causes combined account generally for less than 10 per cent of such bleeders.

Whether or not diagnostic tests can or should be performed depends upon the patient's condition and his clinical course. If surgical intervention is not imminently necessary, gastric suction should be instituted for twenty-four hours to remove the contents of the stomach as well as to reduce the quantity of gastric juice remaining in the stomach. If bleeding recurs, it can make itself known earlier when a suction tube is in place. Thereafter the vigorous medical regimen required negates the use of the gastric tube and its value as a warning sign.

If the patient's condition permits, gastroduodenal fluoroscopy may be performed to diagnostic advantage. The major objection to the early use of this procedure centers about the fear that manipulation will reinstitute bleeding. This fear is probably exaggerated in the minds of many but so also appears to be the case in favor of the fluoroscopy. There is the objection also that the stomach is not emptied of its contents and therefore may obscure the site of the ulcer and lead to misinterpretation of the facts at hand.

Tanner[1] found the gastroscopic examination more useful than fluoroscopy under these conditions. It is his practice to perform this procedure just prior to surgical intervention.

Unless the patient has had previous ulcer symptoms and possibly previous gastroduodenal fluoroscopic examinations, many surgeons prefer to intervene surgically, believing that most lesions which can be diagnosed by fluoroscopy can also be discerned upon direct inspection of the open stomach and/or duodenum. This position can only be justified under emergency conditions and is a trap to be avoided if possible.

PREOPERATIVE SUPPORT

The condition of the patient before operation should be characterized by a normal pulse rate and arterial blood pressure whenever possible. The return to normal of these vital signs does not necessarily guarantee a normal circulating

blood volume, but they are reassuring. The continued administration of blood throughout the operation, maintaining the normal values of these signs, is the simplest test of good blood replacement. A rising pulse rate and a falling blood pressure soon spell disaster in a patient with a history of recent hemorrhage.

Laboratory procedures to include the red cell count, hemoglobin concentration, and hematocrit reading should and can usually be obtained.[2] It must be remembered, however, that the results of these tests in the bleeding patient are likely to disclose too little blood loss rather than too much, as Stewart's studies disclosed.

Blood and plasma volume measurements are very helpful when available, but we can proceed safely with less exact information.

Finally, the chief failure in the preparation of the patient is the administration of too little blood—almost never, too much.

OPERATIVE PROCEDURES FOR THE BLEEDING PEPTIC ULCER

The goal in the surgical management of the patient with the bleeding peptic ulcer is hemostasis. There is general agreement that the operation best suited to this purpose is subtotal gastric resection. This procedure removes the bleeding gastric ulcer but not necessarily the bleeding duodenal ulcer. Care must be taken in the latter instance to excise or to exclude the duodenal ulcer, suturing the bleeding point. In either case it is imperative that the duodenum as well as the remaining gastric segment be opened and carefully inspected for sources of hemorrhage in addition to that from one ulcer.

Because of the earlier high mortality from subtotal resection in the treatment of the bleeding ulcer patient, some have advocated less extensive surgical procedures in the deluded belief that a lesser but satisfactory operation could be concluded without a mortality in the surgical amphitheater when a resection could not. Among the procedures tried have been the excision of the ulcer; when practical, this is the best of the substitutes. Ligation of the left gastric pedicle or oversewing of the ulcer bed are usually unsatisfactory and have been associated too often with recurrence of hemorrhage to encourage their use.

The careful and adequate administration of blood before and during operation enables the surgeon to perform a subtotal gastrectomy with at least the safety of an alternate procedure, and once hemostasis is an accomplished fact the need for haste no longer exists.

If one must intervene surgically and without a definite diagnosis, it is most important to know whether or not the patient experienced massive hematemesis. Hematemesis occurs more often from esophageal or gastric lesions than from duodenal sites. Duodenal massive bleeding is more likely associated with some hematemesis and massive melena.

High gastric resection for massive hematemesis is also the emergency surgical treatment of choice for gastrostaxis, gastric and esophageal varices, or tumor.

If an emergency exploration is indicated for massive hematemesis, "blind" subtotal gastrectomy needs no apology if the decision to operate was correct in the first place.

THE DOCTOR'S DILEMMA: TO OPERATE OR NOT TO OPERATE

The decision to operate upon the patient with a bleeding peptic ulcer is contingent upon several factors. Foremost is his failure to respond to supportive therapy. Other less obvious factors and circumstances must receive their share of consideration. These include the facilities available to the patient in his medical community. The safety with which blood transfusion can be pursued is often as important as the availability of an experienced surgeon and the quality of both vary considerably.

In the past the surgeon has been asked to intervene at a time when the patient's response has made clear that conservative management has failed. With this as the guiding principle for surgical intervention, many patients were moribund when the surgeon was asked to take over. The operative results under these conditions were alarming; mortality rates ranging from 20 to 50 per cent or greater were reported by many and were cause for discouragement to all concerned. Unfortunately, this experience served to strengthen the case in favor of long conservative management when it served better the cause for early surgery, for too often these high mortality figures reflected better the rates of surgical salvage among the medical moribund than they did surgical failure.

Current experience favors the continued application of medical management as the method of choice in treating most patients in an episode of bleeding from peptic ulcer. In support of this view is the fact that 70 to 90 per cent of all ulcer patients who bleed will recover without a second bout of hemorrhage during this episode. Once recovered, if the correction of the patient's ulcer problem seems to be surgical, the procedure of the surgeon's choice can be carried out more easily and within the acceptable mortality rate of less than 3 per cent. The problem now confronting the doctor more often is concerned with the proper selection of the patient for the particular treatment than with its method of administration.

Surgery for the treatment of the bleeding ulcer may be conveniently classed into four categories:

Group I. *Interval surgery* carried out after the patient has fully recovered from his hemorrhagic episode.

Group II. *Emergency surgery* when blood transfusion fails to keep up with blood loss and shock is neither circumvented nor corrected.

Group III. *Urgent surgery* where shock is corrected but bleeding slowly continues. These patients cannot be weaned from their bottle of blood.

Group IV. *Elective intervention* because of the likelihood of a recurrent bout of bleeding during the same episode.

Group I.—The question of interval surgery in the patient with a past history of bleeding is not under discussion here.

Group II.—Emergency surgery is for the patient whose bleeding is so excessive that shock cannot be materially corrected by rapid transfusion. If surgery is to be performed it must be done promptly lest the patient die. Both the operative and nonoperative mortality rates continue high in this group of patients. Many die before they reach the hospital. There is the disadvantage in this group which characterizes any surgery conceived in haste in that it is seldom conducted with the equanimity required. Moreover, the operation is more often one of improvisation than of sound planning. This course of events can be avoided in most instances and converted to one of deliberation if the surgeon will quickly obtain suture hemostasis by opening down upon the ulcer as soon as the abdominal incision is made. Once hemostasis is effected, blood transfusion is rapidly continued until the normal circulatory status is reflected by the pulse rate and blood pressure. From this point on the operation usually can proceed with the dignity of an elective gastrectomy.

Group III.—Urgent surgery is performed in the patient whose circulatory status has been restored but whose bleeding fails to stop. It is this group of patients whose course is difficult to plot because of the many variables that creep into the picture. Among these are the professional skills of the medical community, the duration of bleeding, and the effectiveness of supportive treatment.

Certain "guides" have proved very helpful in the management of patients in this group, but too often these guides have been adopted as "rules of thumb."

The duration of the bleeding is of paramount importance, for the longer the bleeding the greater the opportunity for other complications to assert themselves. Finsterer[3] first called attention to the great difference in results when patients in this category were subjected to operation within the first forty-eight hours compared to those whose surgery was delayed for longer periods of time. The reports of others have been similar and tabulated upon many occasions. The longer the bleeding, the more transfusions needed and the greater the chance for a transfusion accident; the greater also are the opportunities for aspiration pneumonia, anorexia, water and electrolyte imbalance, and for thrombosis and embolic disorders to develop.

Conservative management relies upon blood transfusion and upon antiacid measures to enable the ulcer to heal. Although blood may be available for transfusion, each transfusion carries at least two risks: that of mismatching and that of hepatitis. Although the mortality rate from transfusion is not known in most hospitals, it is a safe assumption that no hospital is without some grief in this connection. For some, the transfusion troubles are greater than for others, and this fact in itself cannot be overlooked in the selection of the treatment to be followed. It is one thing to maintain the circulation with the liberal use of blood and quite another to accomplish it without harm.

Group IV.—The anticipation of recurrence of hemorrhage is in itself often justification for early operation even though there is no evidence of continued

bleeding. Opinions differ as to the weight any given factor should receive in arriving at the decision as to conservation or operative management among the patients of this group. There is, however, general agreement that bleeding tends to recur more frequently under certain circumstances than others. The decision to operate upon such patients is in anticipation of recurrence and is often guided also by factors found in Groups II and III. The decision to operate upon a patient for fear his bleeding may recur implies that the expected operative mortality is less than that anticipated should medical management be continued, taking into account that in many of these patients the expected recurrence of bleeding fails to materialize.

Age of the patient also enters into the decision as to which course to pursue. Patients over 45 years of age tolerate blood loss less well than those in the younger age group. This difference in systemic response to hemorrhage is attributed to the altered resiliency in the arterial bed which occurs with advancing years. However, age is also an important local factor in that the hemostatic benefits attributed to constriction of a severed artery diminish with age and the advances of arteriosclerosis.

The duration of the ulcer history may alter the ability of the bleeding artery to cease just as effectively as does arteriosclerosis. Often the wall of the bleeding vessel is enmeshed in excessive fibrous tissue or its wall is thickened so that it remains open and continues to bleed vigorously. This problem is accentuated when arteriosclerosis is also present; the older the patient the longer he may have had his ulcer disease. When these two conditions are combined with another—that of hypertension, the more conservative approach is that of surgical intervention in most cases, as the rate of recurrence and massive bleeding on conservative management is frequent indeed.

Recurrence of hemorrhage is a more likely probability in gastric than in duodenal ulcer. The vessel eroded in the gastric ulcer usually is of larger caliber than when the more distal branches are the site of hemorrhage as in duodenal ulcer. The recent observation by Dragstedt[4] that gastric ulcer is associated with gastric stasis may also play a role in the increased recurrence rates of hemorrhage from gastric ulcer. Stasis stimulates peptic digestion. It is to be anticipated that clot digestion will take place at rates which are more rapid than when the stomach empties freely and good antiulcer measures, such as frequent feedings and alkaline powders, can be regularly administered.

The stenosed duodenal ulcer which has bled also is recognized as being more susceptible to early recurrence of hemorrhage than when no pyloric obstruction is present. This seems explained on the basis of the long-recognized clinical observation that pyloric obstruction is unfavorable to prompt healing and again because of the difficulties pyloric stenosis imposes upon a sound conservative feeding program.

There remain certain other arguments in favor of resection which are in themselves difficult to classify. One concerns the treatment of a patient with an episode of recurrent bleeding. All are agreed that this patient is a more likely candidate for urgent surgery than he was during his initial bleeding episode if

all other considerations are similar. The choice to remain firm or to intervene surgically needs always to be reviewed in light of the facts at hand and as they concern the individual patient.

Of less consequence in the management of the bleeding gastric ulcer is the question raised as to its nature—benign or malignant. This is the decision for the pathologist to make when he examines the resected specimen or for subsequent studies to reveal once the patient has recovered from bleeding. Hemostasis is the only problem at the time the ulcer is bleeding; all other considerations are secondary.

From this same experience certain errors can be demonstrated to arise when these same "guides" are used blindly as rules of thumb. Some of these are:

1. That the first hemorrhage is seldom fatal and therefore operative intervention is seldom necessary. Blackford[5] observed in his series of patients that deaths from hemorrhage occurred with the bleeding episode in 75 per cent of cases.

2. That death from hemorrhage seldom occurs among patients less than 45 years of age. Fatal hemorrhage does occur in the younger age group but less frequently. In this age group death is more often the result of a massive exsanguinary hemorrhage than of the depleting effects of slower bleeding over a period of several days. Bleeding from a Curling ulcer is especially hazardous.

3. That all patients over the age of 60 whose ulcers bleed should be subjected to surgery promptly. In this older age group the likelihood of recurrence of hemorrhage is somewhat greater than in younger patients. At the same time, so is the mortality of any surgical procedure, as illustrated by Cole,[6] who noted the mortality rate to be four times as great in the older age patients when compared with the younger age group subjected to comparable surgical procedures.

4. That the decision in favor of surgery must always be made within the first forty-eight hours. In some patients the need for surgical intervention is obvious at once as nothing short of an immediate operation will save the life of the patient. In others, bleeding ceases for a few days and may not reappear for a week, at which time the decision as to conservative or surgical management should be reviewed once again.

5. That it is better to undertransfuse and maintain the blood pressure lower than normal if possible, thereby avoiding the possibility of a "blow-out" of the clot lodged in the eroded vessel. This concept is a notion without experimental support. In addition it ignores the ravages of shock which LeVeen[7] showed are likely to be even greater in the case of a bleeding branch of the celiac axis, which reduces to near zero the hepatic artery pressure long before any defection in the systemic arterial pressure appears.

SUMMARY

Experience clearly indicates at this time that no particular set of rules save one can be followed in plotting the course of therapy in the patient with the bleeding ulcer: consider individually the risks and safeguards which opera-

tive and nonoperative managements offer the particular patient in his own medical community. Only then will the maximum in survival rates be achieved, and it should be no less than 95 per cent.

REFERENCES

1. Tanner, N. C.: Personal communication.
2. Stewart, J. D., Sanderson, G. M., and Niles, C. E., Jr.: Blood Replacement and Gastric Reaction for Massively Bleeding Peptic Ulcer, Ann. Surg. 136: 742-751, 1952.
3. Finsterer, H.: Operative Treatment of Severe Gastric Hemorrhage of Ulcer Origin, Lancet 2: 303-305, 1936.
4. Dragstedt, L. R., Oberhelman, H. A., Jr., Evans, S. O., and Rigler, S. P.: Antrum Hyperfunction and Gastric Ulcer, Ann. Surg. 140: 396-404, 1954.
5. Blackford, J. M., and Allen, H. E.: Bleeding Peptic Ulcers, J. A. M. A. 120: 811-812, 1942.
6. Cole, W. H., Schneewind, J. H., and Canham, R.: The Role of Protein Metabolism in Surgery, SURGERY 37: 683-696, 1955.
7. LeVeen, H. H., Mulder, A. G., and Prokop, F.: The Physiological Mechanism for Death in Massively Bleeding Peptic Ulcer, Surg., Gynec. & Obst. 94: 433-442, 1952.

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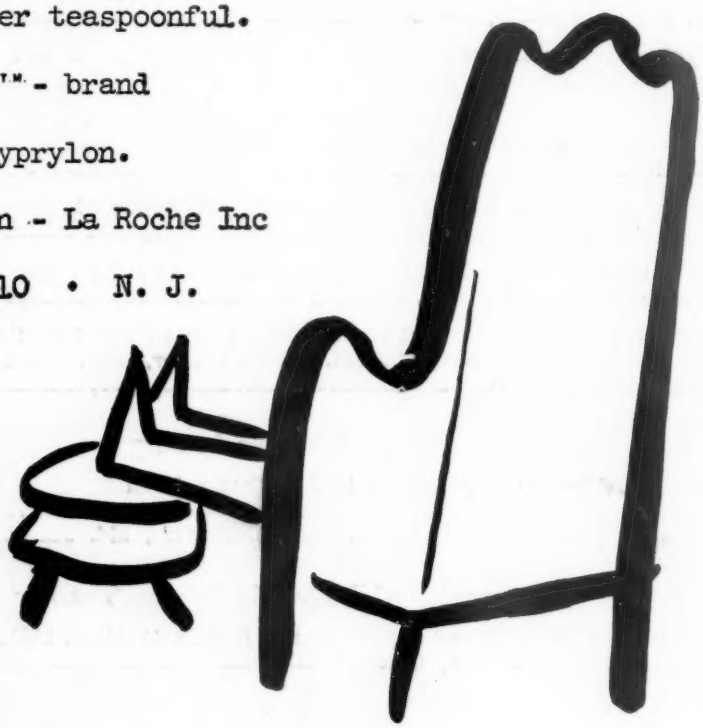
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